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2. Patent application number *(The Patent Office will fill in this part)* — 16 AUG 2003 — 0319321.6

3. Full name, address and postcode of the or of each applicant *(underline all surnames)*

AorTech International plc
Phoenix Cresent
Strathclyde Business Park
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Lanarkshire, ML4 3NJ

07728249001
Patents ADP number *(if you know it)*

If the applicant is a corporate body, give the country/state of its incorporation — United Kingdom

4. Title of the invention — "Valve"

5. Name of your agent *(if you have one)* — Murgitroyd & Company

"Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*

Scotland House
165-169 Scotland Street
Glasgow
G5 8PL

Patents ADP number *(if you know it)* — 1198013 — 00001198015

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Country	Priority application number *(if you know it)*	Date of filing *(day / month / year)*

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11. I/We request the grant of a patent on the basis of this application.

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Murgitroyd & Company

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"Valve"

The present invention relates to artificial heart valves, more particularly to flexible leaflet heart valves which are used to replace natural aortic or pulmonary valves of the heart.

Ideally artificial heart valves should work in a similar fashion to natural heart valves in that when blood flows in a particular direction the valve adopts an open position to permit blood flow through it, whereas when blood tries to flow in the opposite direction the valve adopts a closed position preventing the flow of blood in the reverse direction through the valve (regurgitation).

Natural heart valves use thin flexible tissue leaflets as the closing members. In the closed position the leaflets are arranged such that each leaflet contacts its neighbour. This arrangement serves to close the valve and prevent the back flow of blood through the valve. In the open position

the leaflets separate from each other and move radially towards the inner walls of the blood vessel in which the valve is located. This open configuration of the valve permits the flow of blood through the valve.

A number of artificial cardiac valves have been produced which comprise leaflets which open and close in a similar fashion to natural valve leaflets. However, although the artificial valves work in a similar manner to the natural valves, the geometries of the leaflets differ due to the properties of the materials used in the construction of the synthetic heart valves.

A number of factors have to be considered when designing artificial heart valves of similar design to natural heart valves. These include the pressure gradient required to open and close the leaflets of the valve, regurgitation, blood handling and durability of the valve.

The leaflets of both natural and synthetic heart valves must be capable of withstanding a high back pressure across the valve when they are in the closed position, yet be capable of opening with a minimum of pressure across the valve in the forward direction of blood flow.

This is necessary to ensure correct operation of the valve even when blood flow is low. Further the valve should open quickly and as wide as possible

when blood flows in the desired direction. The maximum orifice of the valve in the open position is generally dictated by the width of the valve.

In order to minimise closing regurgitation (reverse blood flow through the closing valve) in the closed position of the valve, the free edges of the leaflets should come together to form a seal to minimise the reverse flow of blood.

The valve design and the materials used for valve construction should minimise the activation of both the coagulation system and platelets. The flow of blood through the valve should avoid exposing blood to either regions of high shear or relative stasis.

In addition, in order to be suitable for implantation, synthetic valves should be sufficiently durable such that they are clinically functional for at least 20 years. Durability of the synthetic leaflets depends on the materials from which the leaflets are constructed and also the stresses to which the leaflets are subjected during use. Although several materials have suitable hydrodynamic properties, many valves constructed using materials with suitable hydrodynamic properties fail during use, due to fatigue caused by the repeated stresses of cycling from a closed to an open position.

Conventional heart valves typically comprise an annular frame disposed perpendicular to the blood

flow. The annular frame generally has three posts extending in the downstream direction defining three generally U-Shaped openings or scallops between the posts. The leaflets are attached to the frame between the posts along the edges of the scallops and are unattached at the free edges of the leaflets adjacent to the downstream ends of the posts.

A valve design, comprising a leaflet geometry which was elliptical in the radial direction and hyperbolic in the circumferential direction in the closed valve position, with leaflets dip-coated from non-biostable polyurethane solutions onto injection-moulded polyurethane frames has attained durabilities in excess of 800 million cycles during *in vitro* fatigue testing (Mackay TG, Wheatley DJ, Bernacca GM, Hindle CS, Fisher AC. New polyurethane heart valve prosthesis: design, manufacture and evaluation. *Biomaterials* 1996; 17:1857-1863; Mackay TG, Bernacca GM, Wheatley DJ, Fisher AC, Hindle CS. *In vitro* function and durability assessment of a polyurethane heart valve prosthesis. *Artificial Organs* 1996; 20:1017-1025; Bernacca GM, Mackay TG, Wheatley DJ. *In vitro* function and durability of a polyurethane heart valve: material considerations. *J Heart Valve Dis* 1996; 5:538-542; Bernacca GM, Mackay TG, Wilkinson R, Wheatley DJ. Polyurethane heart valves: fatigue failure, calcification and polyurethane structure. *J Biomed Mater Res* 1997; 34:371-379; Bernacca GM, Mackay TG, Gulbransen MJ, Donn AW, Wheatley DJ. Polyurethane heart valve durability: effects of leaflet thickness. *Int J Artif Organs* 1997; 20:327-331.). However, this

valve design became unacceptably stenotic in small sizes. Thus, a redesign was effected, changing the hyperbolic angle from the free edge to the leaflet base, and replacing the injection-moulded frame with a rigid, high modulus polymer frame. This redesign permitted the use of a thinner frame, thus increasing valve orifice area. This valve design, with a non-biostable polyurethane leaflet material, was implanted in a growing sheep model. Over the six month implant period the region close to the frame posts on the inflow side of the valve, at which full leaflet opening was not achieved, suffered a local accumulation of thrombus (Bernacca GM, Raco L, Mackay TG, Wheatley DJ. Durability and function of a polyurethane heart valve after six months *in vivo*. Presented at the XII World Congress of International Society for Artificial Organs and XXVI Congress of the European Society for Artificial Organs, Edinburgh, August 1999. Wheatley DJ, Raco L, Bernacca GM, Sim I, Belcher PR, Boyd JS. Polyurethane: material for the next generation of heart valve prostheses? Eur. J. Cardio-Thorac. Surg. 2000; 17; 440-448). This valve design used non-biostable polyurethane, which had tolerable mechanical durability, but which showed signs of polymer degradation after six months *in vivo*.

International Patent Application WO 98/32400 entitled "Heart Valve Prosthesis" discloses a further design, using closed leaflet geometry, comprising essentially a trileaflet valve with leaflets moulded in a geometry derived from a sphere

towards the free edge and a cone towards the base of the leaflets. The spherical surface, defined by its radius, is intended to provide a tight seal when the leaflets are under back pressure, with ready opening provided by the conical segment, defined by its half-angle, at the base of the leaflets. It is stated that where the spherical portion is located at the leaflet base, an advantage is provided in terms of the stress distribution when the valve is closed and under back pressure.

U.S. Patent No. 5,376,113 entitled "Closing Member Having Flexible Closing Elements, Especially a Heart Valve" issued December 27, 1994 to Jansen et al. discloses a method of producing flexible heart valve leaflets using leaflets attached to a base ring with posts extending from this upon which the leaflets are mounted. The leaflets are formed with the base ring in an expanded position, being effectively of planar sheets of polymer, which become flaccid on contraction of the ring. The resulting valve is able to maintain both a stable open and a stable closed position in the absence of any pulsatile pressure, though in the neutral unloaded position the valve leaflets contain bending stresses. As a consequence of manufacturing the valve from substantially planar sheets, the included angle between the leaflets at the free edge where they attach to the frame is 60° for a three leaflet valve.

U.S. Patent No. 5,500,016 entitled "Artificial Heart Valve" discloses a valve having a leaflet shape

defined by the mathematical equation $z^2 + y^2 = 2RL(x-g) - \alpha(x-g)^2$, where g is the offset of the leaflet from the frame, RL is the radius of curvature of the leaflet at (g,0,0) and α is the shape parameter and is >0 and <1.

A valve design having a partially open configuration when the valve is not subject to a pressure gradient, but assuming a fully-open position during forward flow is disclosed in International Patent Application WO 97/41808 entitled "Method for Producing Heart Valves". The valve may be a polyurethane trileaflet valve and is contained within a cylindrical outer sleeve.

International Patent Application WO 01/41679 discloses a heart valve wherein the leaflets have been designed to facilitate wash out of the whole leaflet orifice including the area close to the frame posts. This Application teaches that stresses are highest in the region of the commisures where loads are transmitted to the stent, but they are reduced when the belly of the leaflet is as low as practicable in the closed valve. To ensure a belly in the leaflet, the above application indicates that there must be sufficient material in the leaflet. Further this application indicates that under back pressure, in the closed position, the shape of the leaflet can be defined by elliptical or hyperbolic coordinates.

A number of designs have been suggested for use in cardiac heart valves to ensure that the heart valves have sufficient leaflet material such that the valve is capable of opening as wide as the maximum possible orifice of the valve, that such opening requires as little energy as possible and further that regurgitation of blood through the valve is minimised.

Previous designs of synthetic heart valves have been based on tissue valves which have different material properties to synthetic materials.

According to the present invention there is provided a cardiac valve prosthesis comprising:

a frame and at least two flexible leaflets;

wherein the frame comprises an annular portion which, in use, is disposed substantially perpendicular to the blood flow, the frame having first and second ends, one of the ends defining at least two scalloped edge portions separated and defined by at least two posts, each leaflet being attached to the frame along a scalloped edge portion and being movable between an open and a closed position,

each of the at least two leaflets having a blood inlet side, a blood outlet side and at least one free edge, the at least two leaflets being in a closed position when fluid pressure

is applied to the outlet side such that the at least one free edge of a first leaflet is urged towards the at least one free edge of a second or further leaflet, and the at least two leaflets being in an open position when fluid pressure is applied to the blood inlet side of the at least two leaflets such that the at least one free edge of the first leaflet is urged away from the at least one free edge of the second or further leaflet;

wherein in a first plane perpendicular to the blood flow axis the length of each leaflet in a circumferential direction (XY) between the posts at any position along the longitudinal axis (Z) of a post is defined by a parabolic function.

Previous designs have not considered the stresses applied to the leaflets during the cycling of opening and closing of the valve.

It is advantageous to provide a synthetic valve leaflet geometry that minimises the stresses present in the leaflets of the valve during cycling from the closed to the open position and back to the closed position in order to increase the lifetime of the synthetic leaflets.

Preferably the length of a leaflet in the circumferential direction (XY) between the posts at

any position along the longitudinal axis (Z) of a post (Z) is defined by the function:

Function of a parabola

$$Y_Z = \left(\frac{4R}{L_z^2}\right)x.(L_Z - x)$$

Wherein Y_Z = Y offset at a particular co-ordinate X and Z

R = parabolic maximum

L_Z = straight line distance between a first post and a second post of the frame at a height Z

x = distance from origin of post towards another post

$$\text{Length} = \int_0^l \sqrt{1+\left(\frac{dy}{dx}\right)^2}\,dx$$

It is understood that a parabolic function includes any pseudotrigonmetric, pseudoelliptical, smooth function or table of values that describe a geometry which is substantially parabolic.

The use of a pseudo function to describe a parabolic function will be obvious to one skilled in the art.

A method of manufacturing a cardiac valve prosthesis of comprising the steps,

providing a model of a model of a heart valve comprising a frame and at least two flexible leaflets,

a) generating loads experienced by at least one heart valve leaflet in use and applying these to the model,

b) determining the stress distribution of the leaflet,

c) changing the circumferential length of the leaflet in XY for any position in Z,

d) determining the new stress distribution of the leaflet,

e) repeating steps C and D to minimise local stress concentrations in the leaflet.

Preferably the method further includes the step of adjusting the model to account for factors which influence the stress distribution of the leaflet during the cycling of the heart valve between an open and closed position.

Preferably the cast shape of the leaflet in the circumferential direction (XY) at any position along the longitudinal axis (Z) of a post is defined by a first wave having a first frequency.

Once the length in XY of the leaflet, in respect of the frame has been determined the cast shape can be defined to allow moulding of the leaflet on a former.

Preferably the first wave is a sinusoidal wave.

More preferably the cast shape of the leaflet in the circumferential direction (XY) at any position along the longitudinal axis (Z) of a post is defined by at least two waves of differing frequencies, which form a composite wave.

Preferably the length of the leaflet in the circumferential direction (XY) between the posts at any position along the longitudinal axis (Z) of a post is defined by a parabolic function and at least one correction factor.

Preferably a correction factor is used to compensate for inward movement of the prosthesis posts on closure of the valve.

Closure of the leaflets, by the backward flow of blood, may cause the posts of the stent to move inwardly to some extent. The posts will typically move inwardly to a greater extent at their tips than where the posts meet the frame.

Preferably a correction factor is used to compensate for stretch in leaflet material on closure of the valve.

Preferably a correction factor is used to compensate for movement in the notional point of coincidence of the leaflets.

Preferably the first wave is asymmetric about the vertical mid plane parallel to and intersecting the blood flow axis of the leaflets.

Preferably the composite wave is asymmetric about the vertical mid plane parallel to and intersecting the blood flow axis of the leaflets.

Preferably the valve comprises three leaflets.

Preferably the frame has first and second ends, the first end defining at least three scalloped edge portions separated by at least three posts, each leaflet attached to the frame along a corresponding scalloped edge portion.

Preferably the three posts are rotationally symmetrically distributed around the circumference of the frame.

Preferably the frame is a collapsible stent.

Preferably the collapsible stent can be delivered to the patient by percutaneous delivery.

More preferably the collapsible stent can be moved from a collapsed to an erect position using an

inflatable balloon when the stent is suitably located in the patient.

According to a second aspect of the invention there is a method of making a cardiac valve prosthesis wherein the method comprises;

- providing a forming element having at least two leaflet-forming surfaces wherein the forming surfaces are such that the length in the circumferential direction (XY) of the leaflet-forming surface is defined by a parabolic function,
- engaging the forming element with the frame,
- applying a coating over the frame and the engaged forming element, the coating binding to the frame, the coating over the leaflet-forming surfaces forming at least two flexible leaflets, the at least two flexible leaflets having a length in the circumferential direction (XY) defined by a parabolic function and a surface contour such that when the first leaflet is in the neutral position an intersection of the first leaflet with at least one plane perpendicular to the blood flow axis forms a first wave having a first frequency,
- disengaging the frame from the forming element.

The leaflets are in a neutral position intermediate to the open and closed position in the absence of fluid pressure being applied to the leaflets.

Preferably there is provided a method of making a cardiac valve prosthesis wherein the method comprises;

- providing a forming element having at least two leaflet-forming surfaces wherein the forming surfaces are such that the length in the circumferential direction (XY) of the leaflet-forming surface is defined by a parabolic function,
- engaging the forming element with the frame,
- applying a coating over the frame and the engaged forming element, the coating binding to the frame, the coating over the leaflet-forming surfaces forming at least two flexible leaflets, the at least two flexible leaflets having a length in the circumferential direction (XY) defined by a parabolic function and a surface contour such that when the first leaflet is in the neutral position an intersection of the first leaflet with at least one plane perpendicular to the blood flow axis forms a composite wave defined by at least two waves of differing frequency,
- disengaging the frame from the forming element.

The application of a wave function to the leaflets in an XY direction is useful in the production of the leaflets.

It is preferred that the stent comprises three posts. In this embodiment a method of making a cardiac valve prosthesis comprises;

- providing a forming element having three leaflet-forming surfaces wherein the forming surfaces are such that the length in the circumferential direction (XY) of the leaflet-forming surface is defined by a parabolic function,
- engaging the forming element with the frame,
- applying a coating over the frame and the engaged forming element, the coating binding to the frame, the coating over the leaflet-forming surfaces forming three flexible leaflets, the three flexible leaflets each having a length in the circumferential direction (XY) defined by a parabolic function and a surface contour such that when the first leaflet is in the neutral position an intersection of the first leaflet with at least one plane perpendicular to the blood flow axis forms a wave defined by at least a first wave, having a first frequency,
- disengaging the frame from the forming element.

The wave applied to the leaflet can be more complicated than a single wave function, where this is the case preferably there is provided a method of making a cardiac valve prosthesis wherein the method comprises;

- providing a forming element having three leaflet-forming surfaces wherein the forming

surfaces are such that the length in the circumferential direction (XY) of the leaflet-forming surface is defined by a parabolic function,

- engaging the forming element with the frame,
- applying a coating over the frame and the engaged forming element, the coating binding to the frame, the coating over the leaflet forming surfaces forming three flexible leaflets, the three flexible leaflets each having a length in the circumferential direction (XY) defined by a parabolic function and a surface contour such that when the first leaflet is in the neutral position an intersection of the first leaflet with at least one plane perpendicular to the blood flow axis forms a composite wave defined by at least two waves of differing frequency,
- disengaging the frame from the forming element.

It will be appreciated by those skilled in the art that leaflets of appropriate lengths and shape can be formed using dip moulding, conventional injection moulding, reaction injection moulding or compression moulding.

Dip moulding can be used to form surgical implants of relatively complex shapes. Typically dip moulding is achieved by dipping a former into synthetic resin or plastic material, removing the former from the synthetic resin or plastics material and allowing the resultant coating of synthetic

resin or plastics material on the former to dry or cure. The moulded article is then removed from the former.

A disadvantage of dip moulding, as described above, is that during the moulding of intricate shapes, bubbles of air frequently become trapped in the cavities or recesses of the mould template. These bubbles of air remain trapped in the moulded article when the article is cured and give rise to holes or pits in the moulded article rendering the moulded article unsuitable for use. Another problem encountered is that of providing an even coating for articles of complex geometry. For example, precision coating is essential for producing surgical implants all of intricate shapes such as prosthetic heart valves. In particular, this problem is encountered when more viscous moulding materials are used for moulding.

Another aspect of the present invention is an apparatus for moulding heart valve leaflets comprising:

(i) at least one platform adapted to hold at least one former;
(ii) at least one housing having an open end adapted to fit over said at least one former;
(iii) sealing means for reversibly sealing said housing to said platform to form a closed

chamber suitable for holding a moulding solution;

(iv) means for inverting said closed chamber;

(v) closeable inlet means for introducing a moulding solution into the closed chamber; and

(v) closeable outlet means for releasing a moulding solution from the housing.

It has been found that by using the apparatus of the present invention to: submerge a former in a moulding solution; invert said former whilst in the moulding solution; and then isolate the former from the moulding solution so that the coating thus formed on the former can be dried or cured, some of the problems of the prior art can be minimised. In particular, inversion of the former whilst in the moulding solution reduces the amount of bubbles formed in the coating. Furthermore, the apparatus of the present invention enables more efficient use of moulding solution and lends itself advantageously to batch processing.

According to another aspect of the present invention there is provided a method of moulding an article using the above-described apparatus comprising:

(i) attaching a former to the platform;

(ii) sealing the housing to said platform to form a closed chamber;

(iii) filling said closed chamber with moulding solution until the former is submerged;

(iv) inverting said closed chamber;

(v) isolating the coated former from the moulding solution by either breaking the seal and raising the platform or by draining the moulding solution from the closed chamber via the outlet means.

Preferably the leaflet is formed from any biostable and biocompatible material.

More preferably the leaflet is formed from Elasteon.

Preferably the former is comprised of at least two portions releasably attached to each other.

Preferably releasable attachment is provided by a screw.

A first portion of the former may be a frame mounting portion and a second portion may be a base portion.

The leaflet as described above with length XY determined by a parabolic function, can be further modified to improve the stress and strain characteristics of the leaflet.

Preferably the method of making a cardiac valve prosthesis further comprises trimming the free edge of at least one leaflet.

More preferably the method further comprises trimming the free edge of at least one leaflet in the longitudinal direction (Z) of the leaflet.

More preferably the free edge of the leaflet is trimmed such that in the longitudinal direction (Z) the free edge of at least one leaflet is parabolic.

Preferably the free edge of at least one leaflet is parabolic in the longitudinal direction toward the second end of the frame such that the maximum depth of the parabolic cut is between 50μm to 1000μm lower than the notional free edge of the leaflet.

Conventional blades are presently used to cut moulded devices formed from plastics or synthetic resin material formed by dip moulding, however these conventional blades become blunted over a relatively short period of time, leading to the production of moulded devices with a poor surface finish on the cut edge.

Preferably the free edge of the leaflet is cut using an ultrasonic cutting device.

Preferably the ultrasonic cutting device comprises

(i) an ultrasonic transducer;

(ii) an elongate blade; and

(iii) attachment means to enable detachable attachment of the blade to the transducer so that, in operation, the transducer causes

the blade to vibrate in a direction along the longitudinal axis of the blade.

It has been found that, for a given ultrasonic frequency, by altering the dimensions of an elongate blade, optimal operation of the cutting device can be achieved. Reducing the amplitude of vibrations perpendicular to the plane of the blade results in a cleaner cut. It has been found that by having a blade of this particular construction precise cutting of synthetic resin and plastics materials can be achieved. The cutting device of the present invention is suitable for cutting acetyls, polyurethane and polymeric materials. The cutting device of the present invention is suitable for moulded surgical implants such as prosthetic heart valves.

Preferably the blade has a width to length ratio of between 0.1 to 0.4. By width means the width of the widest part of the blade and by length is meant the length of the longest part of the blade.

Preferably the elongate blade has a length in the range of 20 to 30 mm, a thickness in the range of 0.5 to 2 mm and a width in the range of 2 to 10 mm. More preferably the width of the blade is between 5 and 8 mm.

Preferably the ultrasonic transducer or motor produces vibrational energy at of a frequency of 15 Hz.

The blade is provided with a terminal end, which is the end furthest away from the transducer, which terminal end may have a single cutting edge and this may be rounded in shape. Preferably the blade has a plurality of cutting edges. Preferably the blade has cutting edges along its longitudinal sides which form a point at the terminal end of the blade, for example in an arrowhead configuration. Preferably, the longitudinal sides are arcuate in shape. In one embodiment the blade is needle-shaped. Preferably the blade is symmetrical in shape about its longitudinal axis.

The blade may be constructed from stainless steel, mild steel or ceramic material. Preferably the blade is constructed from a ceramic material. Ceramic material is harder than steel and remains cooler during operation of the cutting device as there is less heat transfer to the blade.

In another aspect of the present invention there is provided an ultrasonic cutting apparatus comprising

(i) the above-described ultrasonic cutting device;

(ii) a stylus for guiding the blade of the cutting device on the surface of the article to be cut which stylus comprises a rotatable ball bearing mounted on an arm; and

(iii) attachment means for attaching the stylus to the ultrasonic cutting device.

The stylus is positioned so that, in operation, the ball bearing is in contact with the surface of the article to be cut. Preferably the rotatable ball bearing is positioned above, but not in contact with, the terminal end of the blade. Preferably the outer most part of the rotatable ball bearing does not extend to the outermost tip of the terminal end of the blade so that while the ball bearing is in contact with the article to be cut, the cutting edge of the terminal end of the blade penetrates the article by a constant predetermined amount. This results in a consistent and precise cut with each part of the article experiencing the same exposure to the cutting edge of the blade.

The attachment means for attaching the stylus to the ultrasonic cutting device may form part of means for mounting the cutting device on a mounting table. The means for mounting the cutting device on a mounting table may further comprise means such as a 3-axis drive unit for positioning the ultrasonic cutting device relative to the article to be cut.

The ultrasonic cutting apparatus may further comprise a mounting table having a 3-axis drive unit which can move linearly in three directions perpendicular to one another. Preferably the article to be cut is mounted on this drive unit.

According to a further aspect of the present invention there is provided a method of cutting a

heart valve leaflet as described herein using an ultrasonic vibrating blade comprising the steps of,

(i) mounting and fixing a heart valve leaflet to be cut on a mounting table;

(ii) positioning the blade relative to the heart valve leaflet to be cut;

(iii) vibrating the blade;

(iv) moving the heart valve leaflet to be cut relative to the vibrating blade or alternatively moving the vibrating blade relative to the heart valve leaflet to be cut so that the blade cuts the heart valve leaflet to the required shape.

The leaflet has a top and bottom, the bottom of the leaflet being attached to the scalloped portion.

The top of the leaflet may extend beyond the tip of the posts of the frame e.g. by up to 1500 μm from the tip of the posts.

The notional free edge is defined as the free edge of the leaflet prior to trimming. The notional free edge may extend between the posts at a longitudinal height of between 0 to 1500 μm from the tip of the posts.

Preferably at least one leaflet has different thicknesses along a cross section defined by the intersection of a plane perpendicular to the blood flow axis.

More preferably the thickness of the cross section of at least one leaflet in the XY plane, defined by the intersection of a plane perpendicular to the blood flow axis, changes gradually and substantially continuously from a thickest portion where the leaflet is conjoined to the frame to a thinnest portion at the midpoint of the XY plane of the leaflet.

A problem associated with the design of synthetic heart valves is that changing the diameter of the valve or height of the posts of the frame affects the calculation of leaflet geometry. In order to overcome the effects of valve diameter or post heights on leaflet geometry, geometric scaling is typically employed.

Preferably the functions described herein can be used irrespective of valve diameter or the height of the posts of the frame, to obtain suitable leaflet geometry and does not require the use of geometric scaling.

Therefore functions disclosed by the present Application which describe length in the circumferential direction (XY) of a leaflet e.g. the leaflet geometry optimised for a 27mm inside diameter of stent can be used to describe the length in the circumferential direction (XY) leaflet geometry for a stent of different diameter e.g. 17mm inside diameter stent.

This makes the design and manufacture of valves of different diameters more convenient.

An embodiment of the present invention will now be described, by way of example only with reference to the accompanying drawings wherein;

Figure 1a is a plan view of a trileaflet heart valve in the closed position;

Figures 1b, 1c and 1d show plan views of heart valves with 3, 4 or 5 posts in which full closure of the valve is achieved;

Figures 1e, 1f and 1g show plan views of 3, 4 and 5 posted heart valves in which the length XY of the free edge of the leaflets is defined by a parabolic function;

Figure 2a is a perspective view of an embodiment of a trileaflet heart valve of the present invention in a semi-closed position;

Figure 2b is a perspective view of a prior art trileaflet heart valve in a semi-closed position;

Figure 3 is a plan view of an embodiment of a trileaflet heart valve of the present invention in a semi-closed position;

Figure 4a is a plan view of a prior art trileaflet heart valve in a fully open position;

Figure 4b is a plan view of a prior art trileaflet heart valve as shown in figure 4a in a fully closed position;

Figure 4c is a plan view of an embodiment of a trileaflet heart valve according to the present invention in a fully open position;

Figure 4d is a plan view of an embodiment of a trileaflet heart valve according to the present invention as shown in figure 4c in a fully closed position;

Figure 5a is a cross section of the valve as shown in figure 2a along line 3-3;

Figure 5b is a cross section of the prior art valve as shown in figure 2b along line 3-3;

Figure 5c is a cross section of a valve with a sigmoidal shaped leaflet in Z;

Figure 6 is a plan view illustration of an embodiment of a trileaflet heart valve of the present invention;

Figure 7a shows a partial cross section of a post of an embodiment of a trileaflet heart

valve of the present invention in the open position (II) and the closed position (I) of the valve;

Figure 7b shows the a partial cross section of an embodiment of a leaflet of the present invention along the vertical midplane in the open position (II) and closed position (I) of the valve;

Figure 7c shows the a partial cross section of a post of a prior art valve in the open position (II) and closed position (I) of the valve;

Figure 7d shows the a partial cross section of a leaflet of a prior art valve along the vertical midplane in the open (II) and closed (I) position of the valve;

Figure 8a shows the principal stress envelope present in a prior art heart valve leaflet;

Figure 8b shows the strain energy release present in a prior art heart valve leaflet in the X axis from a closed to open position;

Figure 8c shows the strain energy release present in a prior art heart valve leaflet in the Y axis from a closed to open position;

Figure 8d shows the resultant strain energy release present in a prior art heart valve during cycling from a closed to open position;

Figure 9a shows the principal stress envelope present in an embodiment of a heart valve according to the present invention;

Figure 9b shows the strain energy release present in an embodiment of a heart valve according to the present invention in the X axis from a closed to open position;

Figure 9c shows the strain energy release present in an embodiment of a heart valve leaflet according to the present invention in the Y axis from a closed to open position;

Figure 9d shows the resultant strain energy release present in an embodiment of a heart valve leaflet according to the present invention during cycling from a closed to open position;

Figure 10 is an illustration of an embodiment of one leaflet according to the present invention;

Figure 11 is a diagrammatic representation of a prior art leaflet moving from a semi-closed (a) to successively more open position (b) and (c)

to a fully open position (d) illustrating the formation of a bubble or buckle;

Figure 12 illustrates the shape of the leaflet being defined by a first wave further to determination of the circumferential length of the leaflet;

Figure 13 is graph of Cardiac Output (l/min) against mean Pressure Gradient (mmHg);

Figure 14a shows a sectional view of dipping apparatus prior to moulding;

Figure 14b shows a sectional view of apparatus post moulding;

Figure 14c shows a cross sectional view of a former suitable for use in the moulding apparatus of the present invention;

Figure 15 a perspective view of an ultrasonic cutting device mounted on a mounting table;

Figure 16 a view of the cutting apparatus of an ultrasonic cutting device;

Figure 17 a perspective view of an ultrasonic cutting apparatus according without a stylus; and

Figure 18 a side view of ultrasonic cutting apparatus without a stylus.

As previously discussed, a number of designs have been suggested for use in cardiac heart valves to ensure that the heart valves have sufficient leaflet material such that the valve is capable of opening as wide as possible to the maximum orifice of the valve, and that such opening requires as little energy as possible and further that regurgitation of blood through the valve is minimised.

In order to minimise the regurgitation of blood it has been suggested that the free edge of the valve is spherical in geometry to ensure that the free leaflet edges are able to come together and seal against one another.

US Patent 5,500,016 discloses a leaflet defined by the equation:

$$z^2 + y^2 = 2RL\ (x-g) - \alpha(x-g)^2$$

to describe the geometry of the leaflets. As Z, defines the shape of the leaflet in the blood flow axis and as Z is defined as z^2 then a leaflet defined by the above would have a spherical geometry in the axis parallel to blood flow. International Patent Application WO 98/32400 discloses that spherical surfaces at the leaflet edges seal more effectively than planar or conical surfaces. International Application WO 01/41679 discloses that

stresses are highest in the region of the comissures where loads are transmitted to the stent, but they are reduced when the belly of the leaflet is as low as practicable in the closed valve.

In addition, International Application WO 98/32400 also suggests that it is advantageous to provide a spherical portion of leaflet adjacent to the base of the leaflet as it confers advantages in the stress distribution when the valve is closed and pressure is greater downstream than upstream.

The prior art teaches that leaflets of heart valves should have considerable excess material in the vertical axis Z, parallel to the blood flow to enable a suitable seal to be achieved at the free edge of the leaflet and to reduce the stress present in the leaflet during open and closing.

As shown in figure 1b, 1c and 1d, the use of a frame comprising 3, 4 or 5 posts induces different angles θ in the valve leaflets, to ensure a close fitting tight seal of the leaflets, which minimises regurgitation of blood through the valve. As the number of posts increases, the smaller the angle θ and the more bent the leaflets are at a particular point. In cycling between the open and closed position, the valve will undergo considerable flexing, particularly at angle θ, the smaller the angle θ, the greater the stress experienced by the valve at this point and the more the likely the valve is to fail due to stress.

The material properties of tissue, which has low stress at low and moderate strain means tissue valves are more able to cope with such flexing than synthetic materials. Synthetic materials typically have different stress to strain relationships than tissue and higher stress is typically experienced by these materials at low and moderate strains. This means that flexing is more likely to cause damage to leaflets constructed from synthetic material than tissue material.

Previous valve designs have been largely based on tissue valves and have not taken account of the different material properties of tissue.
In contrast to previous designs and teaching concerning valve construction, which was driven by the supposed need to obtain a close fitting seal of the leaflets, particularly at the free edge, the leaflets of the present Application were designed to minimise the stress experienced by the leaflet during cycling between the open and closed position.

To reduce the sharp curvature, which promotes stress points at specific points along the free edge, the length of the free edge (XY) of the leaflet was determined using a parabolic function. The parabolic length of the free edge can be determined by using the distances between the posts of the frame where the free edge is conjoined to the posts and the parabolic maximum.

As shown in figures 1e, 1f and 1g the use of a parabolic shape at the free edge results in a gentler curvature of the leaflets and enables the length of the material along the free edge to be determined from a knowledge of the frame dimensions. However, this design, contrary to previous teaching, does not allow a close fitting to be achieved between the leaflets at all points along the free edge. Surprisingly, the seal obtained between the leaflets using a parabolic or like function is sufficient to minimise regurgitation of blood through the valve to the required degree for the valve to be effective.

The determination of the length XY at the free edge of the leaflet is important to ensure that closure of the leaflets is achieved and to minimise the excess material of the leaflets at the free edge such that the free edges of the leaflets do not fold over each other in the closed position.

In addition to allowing determination of the length of XY at the free of the valve, the present Application also allows determination of the XY lengths of the leaflets at all points in Z by using a parabolic function to determine the shape of the leaflets at all points in Z.

As shown in figures 5a, 5b and 5c, in the closed position, the leaflet can be substantially linear (figure 5a), have excess material such that a belly forms (figure 5b) or have reduced XY lengths of the

leaflet towards the base such that the leaflet forms a generally sigmoidal shape (figure 5c). In both figures 5b and 5c the XY lengths of the leaflet and thus the leaflet shape would be determined using a non-continuous function.

The belly in the valve as shown in figure 5b would create increased stress in the belly region. In figure 5c the reduction of material in XY towards the base of the posts would promote an increase in the stress concentration at the portion of the leaflets towards the free edge.

By determining the lengths XY of the leaflet as a parabolic function or the like at each point in Z, such that the XY lengths in Z vary as a continuous function, localised stress concentrations can be minimised and a more uniform stress distribution across the leaflet achieved.

As shown in figure 1a and figure 2a, a preferred embodiment of the heart valve prosthesis 8 of the present invention comprises a stent or frame 10 which is substantially cylindrical. The frame has a first end 12 and second end 14. The first end 12 comprises three scalloped edge portions 16a, 16b and 16c separated by three posts 18, each post having a tip 20. The cardiac valve further comprises three leaflets 30. Each leaflet 30 has a fixed edge 32 joined to a respective scalloped edge 16a, 16b or 16c of the frame 10 and a free edge 34 which extends substantially between the tips 20 of the posts 18.

The leaflets 30 are configured to be movable from an open to a closed position and from a closed to open position. In an aortic position (when the prosthesis is positioned at the site of the aortic valve), the leaflets 30 have a blood inlet side 36 and a blood outlet side 38 and are in the closed position when fluid pressure is applied to the outlet side 38 i.e. by the blood of the aortic artery and in the open position when fluid pressure is applied to the inlet side 36 i.e. by the blood of the ventricle. The leaflets are in a neutral position intermediate to the open and closed position in the absence of fluid pressure being applied to the leaflets.

Where the valve is being used in a mitral position, between the left atrium and left ventricle of the heart, the orientation of the valve is the opposite to that described above such that blood flow from the left atrium moves the leaflets to an open position, the leaflets opening towards the left ventricle to allow blood to flow into the left ventricle. Back pressure from blood flow from the left ventricle towards the left atrium causes the mitral valve to close to minimise regurgitation.

In figure 5b which is a sectional view along line 3-3 illustrating the closed position of a leaflet of a valve of the prior art, a 'belly' portion 40 exists in the mid portion of the leaflet. This 'belly' portion between the free edge and the central

portion of the leaflet causes leaflets of the prior art to have a double curvature, a curve in XY and a curve in Z. Further, the 'belly' shape 40 causes leaflets of the prior art to be almost concave in shape when viewed in cross section along the vertical midplane of the leaflet.

As shown in figure 5a, which is a sectional view of the valve of the present invention along line 3-3 as shown in figure 2a, no 'belly' is present in the leaflets and in Z the leaflet in the closed position is substantially linear.

The conventional design including a 'belly' portion was previously favoured as it was thought to maximise sealing of the valve at the free edge and minimise regurgitation.

However, the double curvature, which comprises curvature in XY plane and in Z plane results in excess leaflet material at both the open and closed position which promotes the formation of a bubble or buckle 50 in the leaflet material (as shown in figure 11) during movement from a closed to open position.

This excess material is shown most clearly by comparing figure 7d which shows a cross section of the valve along the vertical midplane (line I-I of figure 2b) of the leaflet 30 parallel to the blood flow axis in a prior art leaflet with figure 7b which shows a cross section along the vertical

midplane (line I-I of figure 2a) of a leaflet of the present invention. This comparison clearly shows that the leaflet 30 of the present Application does not display a belly region 40. Indeed the cross section shown in figure 7b indicates that the leaflet shape of the present invention is substantially linear in the vertical direction in both the open and closed valve positions.

To determine the circumferential length of material in XY to remove the 'belly' 40 observed in prior art leaflets, the length in the circumferential direction (XY) of the leaflet for any position in z must be determined, which still allows suitable opening and closure of the valve.

As shown in figure 6 the material of the leaflet must extend between the posts 18 such that in a closed position the free edge of the leaflets 34 come together at point 42 to minimise regurgitation of blood through the valve.

This circumferential length (XY) can be mathematically defined using a parabolic function.

Function of a parabola

$$Y_z = \left(\frac{4R}{L_z^2}\right) x . (L_z - x)$$

Wherein Y_z = Y offset at a particular co-ordinate X and Z

R = parabolic maximum

L_Z = straight line distance between a first post and a second post of the frame at a height Z

X = distance from origin of post towards another post

To calculate the circumferential length (XY) at a height point of the posts for a leaflet defined in the circumferential (XY) direction by a parabolic function the following function can be used:

$$\text{length of parabolic curve} = \int_0^l \sqrt{1+\left(\frac{dy}{dx}\right)^2}\, dx$$

This allows a circumferential length (XY) to be determined at each height point in Z.

Thus as shown in figure 10 the circumferential length (XY) can be determined at Z1, Z2, Z3 ...Zn.

The length of the leaflet in the circumferential direction (XY) is calculated and repeated in the radial direction (Z) to provide the complete geometry of the leaflet.

As the scallop edge 32 of the frame 10 as defined by the posts 18 of the frame can be determined by measuring the frame, then a leaflet 30 can be defined by determining the distance between the two posts 18 at several height points in Z (where Z is a particular height along the posts). This post to

post distance can then be used in the equation detailed above to generate a parabola (P) at each height point. In the embodiment shown, due to the scallop shape 32 defined by the posts 18 the circumferential length of the leaflet in XY will decrease moving from the first end at the tip 20 of the posts toward the second end of the frame 14 at the base of the posts. The more height points which are chosen, the more lengths (P) which can be calculated along Z. If a large number of height points are chosen the lengths determined by the parabolic function moving from the tip of the posts to the base will vary in a substantially linear fashion.

The leaflets 30 of a valve 8 which are of circumferential length (XY) as determined using the above parabolic function will meet at the free edge 34 of the leaflet 30, but will not meet significantly at points lower than the free edge 34. The meeting of the leaflets at the free edge allows regurgitation to be minimised without including excess material or a belly region 40 in the leaflets 30.

The circumferential length (XY) can be further adjusted to take account of factors which occur during cycling of the heart valve. These factors include inward movement of the posts 18 of the frame 10 due to pressure on the leaflets 30 during closing of the valve. The amount of inward movement of the posts 18 of the frame 10 is influenced by the

rigidity of the frame 10 and the pressure exerted on the valve. The tips 20 of the posts 18 of the frame 10 move to a greater extent than the base of the posts and as the scallop geometry between the posts 18 of the frame 10 is accurately known this differential movement can be taken into account when determining the optimal circumferential length (P) of XY in the leaflet 30.

In addition to the posts 18 of the frame 10 moving toward each other during closure, the posts 18 also move towards the centre point 42 where the leaflets meet or the point of coincidence. The circumferential length XY of the leaflet can be adjusted to account for this movement.

The material of the leaflet 30 typically has some degree of elasticity and will stretch in response to blood flow pressure. This stretching can again be taken into account in determining the lengths of the leaflet 30 to ensure that a belly region 40 of the valve is minimised.

As shown in figure 8a, analysis of the stresses over time incurred by heart valves during the cycling process has revealed that the principal area of stress 60 in existing cardiac valves is found close to the midpoint of the free edge of the leaflets.

Using the data from figure 8a, strain energy release in X and Y, as shown in figures 8b and 8c respectively can be determined. Figure 8b shows

that leaflets of the prior art have a vertical predisposition to defect propagation 62 at the free edge 34. Figure 8c indicates that leaflets have a predisposition to defect in the lateral dimension, at an area 64 in the leaflet 30 lower than the free edge of the leaflet 34, the lower area being located above the central portion of the leaflet. In tests during cycling of cardiac valves it has been found that over time, the stress in this lower area promotes failure of defects in the material to occur. These defects can cause valve failure.

The present invention has shown that analysis of the dynamics of existing valves during the cycling process has determined that the stress in this lower area is caused by the leaflets requiring to change the direction of their surface curvature during cycling.

In particular, as shown in figure 11, on cycling from a closed to an open position a region lower than the free edge forms a bubble like formation or buckle 50 on the surface of the leaflet which is opposite in direction to the curvature of the surface of the rest of the leaflet.

On moving from the closed to open position, the bubble like formation 50 is forced to become inverted such that it projects in an opposite direction causing a whip like action in the leaflet 30. This whip like action promotes high stresses in

the area lower than the free edge 34 of the leaflet, as shown in figures 8a, 8b, 8c and 8d.

The inventor has surprisingly determined, as shown in figure 9a, that the principal stress envelope in relation to the valve as described in the present application, wherein the circumferential length XY of the leaflet at any point in Z is defined as a parabolic function, is decreased across the whole of the valve. In particular strain energy release in X and Y, as shown in figures 9b and 9c respectively, in relation to the valve of the present invention indicates that a leaflet wherein the circumferential lengths XY are determined by a parabolic function has minimised predisposition to defect propagation in the lateral dimension at an area in the leaflet lower than the free edge of the leaflet and above the central portion.

A reduction in the predisposition to defect propagation in the lateral dimension at an area in the leaflet between the free edge of the leaflet and the central portion in the leaflet of the present invention is observed because there is less excess material and thus minimal belly in the leaflet of the present design.

On moving from the closed to open position a bubble like formation 50 is no longer created and thus a whip like action does not occur in the leaflet. As discussed, it is this whip like action which has been determined to promote high stresses in the area

lower than the free edge of the leaflet. As illustrated by comparing figures 8a and 9a, in contrast to the valves of the prior art, uniform principle stress distribution, is observed across the surface of the leaflet of the valve described in the present Application.

Minimisation of the regions of stress in the leaflet, during cycling of the leaflet, will increase the durability of the leaflet.

Use of a parabolic function to determine the circumferential lengths XY of the leaflet at each height point in Z causes the vertical distribution of lengths of the leaflet to be substantially linear at the fully open and closed position.

It will be appreciated by those in the art that other functions with the addition of suitable modifying factors could be used to derive a function which substantially describes a parabola and which leads to the vertical distribution of lengths of the leaflet to be substantially linear at the fully open and closed position, but which is based on for instance an elliptical function.

As discussed, additional parameters may be included in the parabolic function used to determine the circumferential lengths XY of the leaflet. These additional factors may account for movement in the posts of the stent, elasticity of the leaflet material during movement of the leaflets from a

closed to an open position or other factors which occur during cycling which influence the length of the leaflet require to allow closure.

The function described above explicitly determines lateral lengths of the parabolic curve at any height point in Z which is along a post of the frame. In view of this the above function can be applied to any diameter of valve or valves with different heights of posts, without the need for geometric scaling. This means that different dimensions of valves can be manufactured with the same leaflet geometry without further undue experimentation.

The surface contour of the leaflets 30 of the embodiment described are such that in a fully open position, the intersection of the leaflets of the valve perpendicular to the blood flow axis, forms a substantially cylindrical shape.

In addition to the above, it has also been determined that stress at the free edge of the leaflet, as shown in figure 8a, can be further reduced by trimming the free edge 34 of the leaflet in the longitudinal direction (Z) such that the free edge is substantially parabolic 70, with the maximum depth of the parabola being furthest from the notional untrimmed free edge 74. The maximum depth of the parabola is generally located at the midpoint of the free edge 72 (figure 9a). Figure 9a shows the effect of introducing a parabolic curve in the vertical direction of the free edge. Comparison of

figures 8b, 8c and 8d with 9b, 9c and 9d shows that the strain energy release at the free edge is significantly reduced through the introduction of the parabola in the longitudinal direction (Z).

Ideally the notional free edge 74 is trimmed in a parabolic curve, wherein the maximum depth 72 of the parabola 70 is between 50μm to 1000μm lower than the notional untrimmed free edge 74.

A different shape of cut, trim or notch can be introduced in the free edge to decrease the stress at the free edge. However, particular shapes of cuts, trims or notches may introduce defects into the leaflet which would decrease the leaflets durability to stress. A parabolic trim as described is therefore advantageous in that focal points of stress are not introduced to the free edge of the leaflet. Cuts, trims and notches which do not create bending stresses at localised points on the free edge are preferable.

In one embodiment a parabolic cut may be made using an ultrasonic cutting device. As shown in figure 1 in one embodiment the ultrasonic cutting device comprises an ultrasonic transducer (100); a blade (110); and attachment means (120) to enable detachable attachment of the cutting blade to the transducer. The blade has two arcuate cutting edges which meet at a point to form the terminal end of the blade. In this embodiment the stylus is not

present. The ultrasonic cutting device is mounted on the mounting table (130) by means of a clamping assembly (140). The clamping assembly includes an upright member (150) that extends from a first end perpendicularly from the mounting table, a support member (160) that extends laterally from the upright member and is held relative to the upright member by a fixing block (170), and a clamp (180) which secures the ultrasonic cutting device to the clamp support member. The clamp support member is slideably moveable up and down a portion of the upright member by turning of an adjusting screw (190). In addition, the clamp support member is slideably moveable laterally in relation to the upright member, this movement being effected by the rotation of a second adjusting screw (200). The clamp support member is located between the fixing block and a securing plate (210). The securing plate can be moved towards the upright member to secure the clamp support member at a suitable position.

As shown in figure 16 an arm (220) can extend from the clamp (180) to the cutting blade. A ball bearing (222) is rotatably mounted at one end of the arm and is positioned just above, but not in contact with, the blade. In use the ball bearing is in contact with the surface of the article to be cut and its position controls the extent of blade penetration into the article.

Figure 17 shows a perspective view of the cutting apparatus in position for operation without the

stylus guide. The heart valve leaflet to be cut is mounted on a 3-axis drive unit (230). This drive unit may be driven by electric motors. Figure 18 is a side view of the embodiment shown in figure 17.

In the embodiment of Figures 17 and 18, movement of the drive means causes the heart valve leaflet to be cut to be brought into contact with the blade. By accurate positioning of the heart valve leaflet to be cut, the cutting process may be accurately repeated. A set pattern can then be followed and may be instructed by a computer which drives the drive means.

Leaflets of the geometry described herein can be produced using methods known in the art such as injection moulding, reaction injection moulding, compression moulding or dip moulding.

In one embodiment the heart valve leaflets may be made by dip moulding. As shown in figure 14a the dipping apparatus may comprise a platform (1000) holding a former (1110). A housing (1130) is sealed to the platform to form a closed chamber (1140). The housing comprises side walls (1150) and a ceiling (1160) and is provided with inlet means (1170) which can be closed by valve (1180).

The platform is adapted to hold at least one former. Preferably the platform is adapted to hold one former. By hold means the former is secured to the platform so that it will remain in place even upon

inversion or rotation of the platform. Preferably the former is releasably held on the platform.

The former has a shape so that when coated with the moulding solution it will produce an article of the desired size and shape. The former may comprise a core holding a frame which when coated with the moulding solution will produce a leaflet of the desired size and shape.

In a preferred embodiment, the former (1110) is of two-part form, as is shown in Figure 14C. The former comprises a frame mount (1112) fixed to a base portion (1114). A frame 8, for a heart valve prosthesis, can be mounted on the frame mount 1112. The frame mount is fixed to the base by fixing means for example a screw (1116) or any suitable fixing means such as a bayonet fitting or push fit fitting. The frame mount is removable from the base portion.

A frame mount and base portion, (two part former) may be used during leaflet construction, the frame mount being suitably shaped to a frame to be mounted on the frame mount and allow the production of the leaflets by dip moulding. The frame mount can also be used to hold the frame and leaflets during subsequent cutting of the valve leaflets. The frame mount is releasably attachable to the base former portion such that the frame mount portion can be removed from the base portion so that the base portion may be reused. The frame mount portion may be releasably attachable to the base portion by a

screw. Should the frame mount be damaged during the cutting stage the frame mount can be discarded while retaining the base portion and thus only a part and not the entire former need be replaced. In addition, different types of former mounts capable of mounting frames of different diameters or with different valve leaflet shapes can be fixed to the same base portion thus reducing the need for complete formers.

The housing (1140) has an open end (1142) so that when placed on the platform (1000) the former can extend into the housing.

The housing is of a shape and size so that it fits over the former (1110) and has the capacity to hold enough moulding solution to coat the former. The housing has a ceiling (1160) which is the part of the housing opposite to the platform. The housing may have any suitable shape, for example it may be a cylinder having one closed and one open end, with its closed end being the ceiling.

Typically the platform and the housing are constructed from steel.

The apparatus is provided with means for inverting the closed chamber. The inverted and open chamber is shown in figure 14b. Invertion of the housing may be provided by means for rotating the platform about a horizontal axis. In one embodiment, the platform is rotatable about a horizontal axis

through the horizontal plane of the platform. This may be achieved by having the platform pivotally supported on a frame. The frame may comprise lateral pins which extend laterally from the frame into the platform so that the platform can rotate around them. In an alternative embodiment, the housing is rotatable about a horizontal axis in the horizontal plane of the open end of the housing. This may be achieved by having the housing pivotally supported on a frame. The frame may comprise lateral pins which extend laterally from the frame into the housing so that the housing can rotate around them.

Preferably inversion of the closed chamber is effected by drive means including a hand crank and an electric motor.

The closed chamber has closeable inlet means for introducing the moulding solution to the closed chamber. The inlet means may be closeable by means of a valve. The inlet means are preferably an opening in the ceiling of the housing and are provided with a pipe in connection with a central reservoir of moulding solution. In one embodiment the platform is provided with the inlet means. The inlet means may alternatively be provided in one of the side walls of the housing so that it will be in a position close to the platform in the closed chamber. In this embodiment the moulding solution may be pumped from a reservoir into the closed chamber via the inlet means. This latter embodiment

is preferred when more viscous moulding materials are being used.

Preferably the inlet means and/or the outlet means are heated. The moulding solutions generally used in the moulding of surgical implants are generally viscous in nature and this viscous nature can make the movement of the moulding solutions through the inlet and outlet means difficult to achieve. Heating means can be incorporated in the moulding apparatus and used to heat both the housing and the inlet and outlet means. The raised temperatures of the moulding solutions make these solutions less viscous allowing easier movement of the solutions through inlet and outlet tubes.

The housing has closeable outlet means. Preferably an opening/pipe in the ceiling of the housing forms the outlet means. When the housing is inverted then the moulding solution can be drained through such an opening/pipe under the force of gravity. The outlet means may be closeable by means of a valve.

Preferably, as in the embodiment shown in Figures 14a and 14b, the outlet means is also the inlet means.

In operation, a former is releasably secured to the platform and a housing is placed over the former and sealed to the platform. The closed chamber thus formed should be in a position whereby the former is upright. Moulding solution is introduced into the

chamber through the inlet means until it reaches a level above the former, e.g. level (1152) indicated in Figure 14a. At this stage the inlet means is closed by means of valve (1180). After a suitable period of time, the platform, and thus the closed chamber, is inverted by rotating, in this case, the platform around a horizontal axis. The inverted chamber is then left for a suitable period of time before the housing/platform seal is broken and the housing is lowered. This exposes the now-coated former in an inverted position. This can be seen in Figure 14b. The moulding solution can then be drained from the housing using the inlet means (1170) which doubles as outlet means in this embodiment. Alternatively the moulding solution can be drained from the housing before the housing/platform seal is broken. The coating on the former can now be dried/cured/treated appropriately.

As the closed chamber is a sealed system it is possible to exchange the air present in the interior of the closed chamber, when moulding solution is not present, with another solution or gas. The type of solution or gas with which the mould chamber can be filled prior to introduction of moulding solution can be chosen in line with manufacturing requirements. In this way, contact between the mould solution and moisture in the air can be avoided.

In one embodiment the apparatus comprises a plurality of platforms and a plurality of housings.

In this embodiment, preferably all the inlet means are in connection with a central reservoir of moulding solution, with the inlet means and the reservoir forming a manifold. Preferably the manifold is heated. In this embodiment, preferably all the platforms are pivotally supported as a unit on a frame or all the housings are pivotally supported as a unit on a frame. Batch moulding carries the advantages of having greater consistency of results and of being more cost effective.

The above dipping procedure and apparatus can be used, but is not limited to the production of heart valve leaflets which can be produced for dip moulding.

As discussed the circumferential length XY of the leaflet at any height point in Z along the post of the frame is explicitly provided by a parabolic function or a pseudo function used to describe a parabolic function. As is clear from figures 1e, 1f and 1g, the manufacture of valve leaflets in the closed position, as described herein, by dip moulding or injection techniques would be difficult as the free edges of the leaflets contact each other. Although a former could be provided in which the valve leaflets were produced in the open position, it is more desirable to form the leaflet in a neutral position between the two extremes of fully open or fully closed.

One method of forming the leaflets is to determine the length of the leaflet in the XY direction for each point in Z for a preferred shape of leaflet.

On determining the length of the leaflet at each point in Z to minimise the formation of a belly in the leaflet and using appropriate correction factors to determine a final XY length at that point in Z, a wave function can be applied to the leaflet at that point in Z. As shown in figure 12 the wave function will change the shape of the leaflet at that point in Z from a parabolic curve to a desired cast shape, but the length of the leaflet as determined by the initial-parabolic shape will be maintained and following manufacture of the valve, closure of the valve, will cause the leaflet to adopt a parabolic shape again at each point in Z.

The wave shape of the leaflet is used to provide a former element with leaflet forming surfaces of the shape as defined by the waves arranged in Z for casting of leaflets.

The valve is thus produced such that in a cast position the leaflet is in neutral position, intermediate the open and closed position in the absence of fluid pressure being applied to the leaflets. Production of the valve in the neutral position means that the leaflets are substantially free of bending stresses in this position.

The shape of the former, on which the leaflet is formed, can be defined by one wave function, or several wave functions which together form a composite wave.

Regardless of the wave function used for the casting of the leaflet, the length of the leaflet is defined at each point in Z along the post of the scallop by a parabolic function or pseudo parabolic function as described above together with any correction factors.

The shape of the inner surface of the leaflets will substantially replicate the shape of the former. The shape of the outer surface of the leaflets will be similar to the shape of the inner surface, but variations will result e.g. from the properties of the polymer solution and techniques used to create the leaflet.

The leaflets of suitable length as defined by the parabolic function and any correction factors and of shape as defined by either a single or composite wave function are attached to a suitable frame. The construction of a suitable frame will be obvious to those skilled in the art. The frame can be made of a biocompatible polymer, metal or composite. The frame can be coated with polyurethane to allow integration of the leaflets.

Further to describing a first leaflet using the above function, the remaining two leaflets of this

three leaflet embodiment can be determined by rotating the geometry about the Z axis through 120° and then through 240°.

Having formed the leaflets of the valve as described above these can then be trimmed such that the edge of the leaflet not attached to the frame extends horizontally between two posts horizontally between a longitudinal length 0 to 1500μm beyond the tips of the posts of the frame. The edge of the leaflets which extends horizontally between the tips of the posts or between a longitudinal length 0 to 1500μm beyond the tip of the posts is deemed to be the notional free edge of the leaflets.

The notional free edge of the leaflet can be further trimmed in the longitudinal direction such that a parabolic curve is introduced, the maximum depth of the parabola being located between 50μm to 1000μm opposite the notional untrimmed free edge toward the portion of the leaflet which attaches the leaflet to the scallop portion of the frame.

As shown in figure 13, surprisingly, in addition to reducing the lateral stress of the valve, determination of the length of the leaflet at each point in Z according to a parabolic function not only minimises the formation of a belly in the leaflet, but also reduces the pressure gradient required to open the valve from a closed position.

The opening of a cardiac valve to as wide an orifice as possible under minimal pressure gradients is a key parameter in the design of synthetic heart valves.

A valve of the present invention may be used in any required position within the heart to control blood flow in one direction, or to control flow within any type of cardiac assist device.

Modifications and improvements can be incorporated without departing from the scope of the invention.

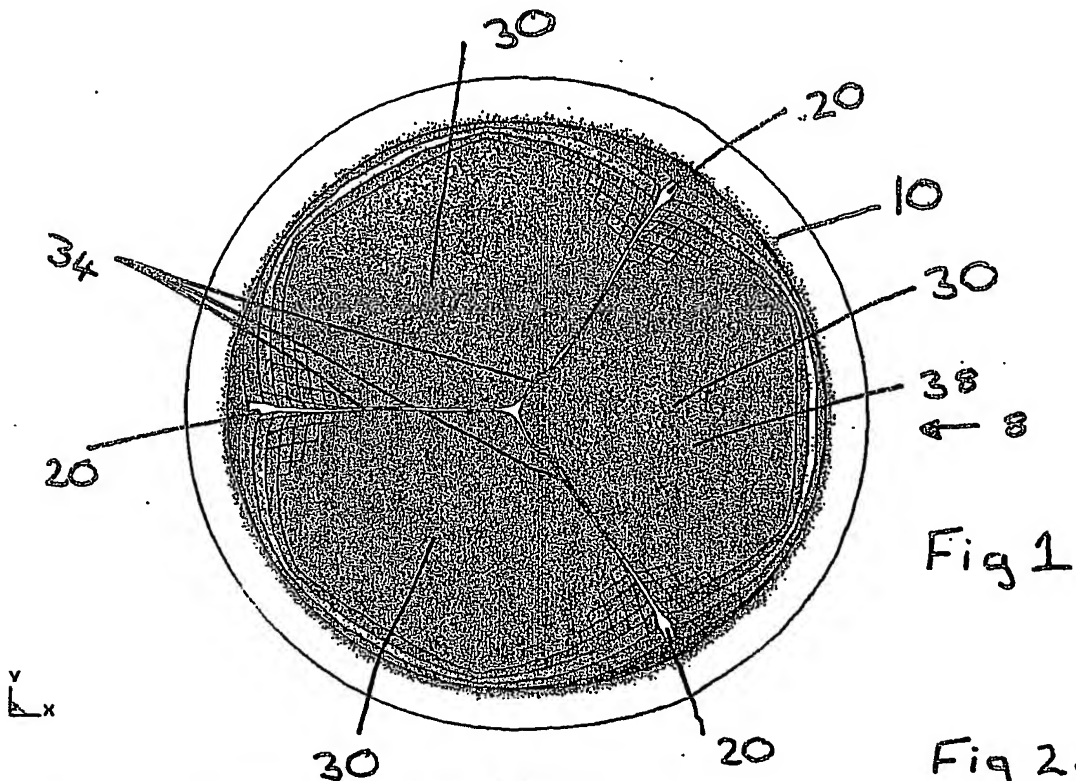
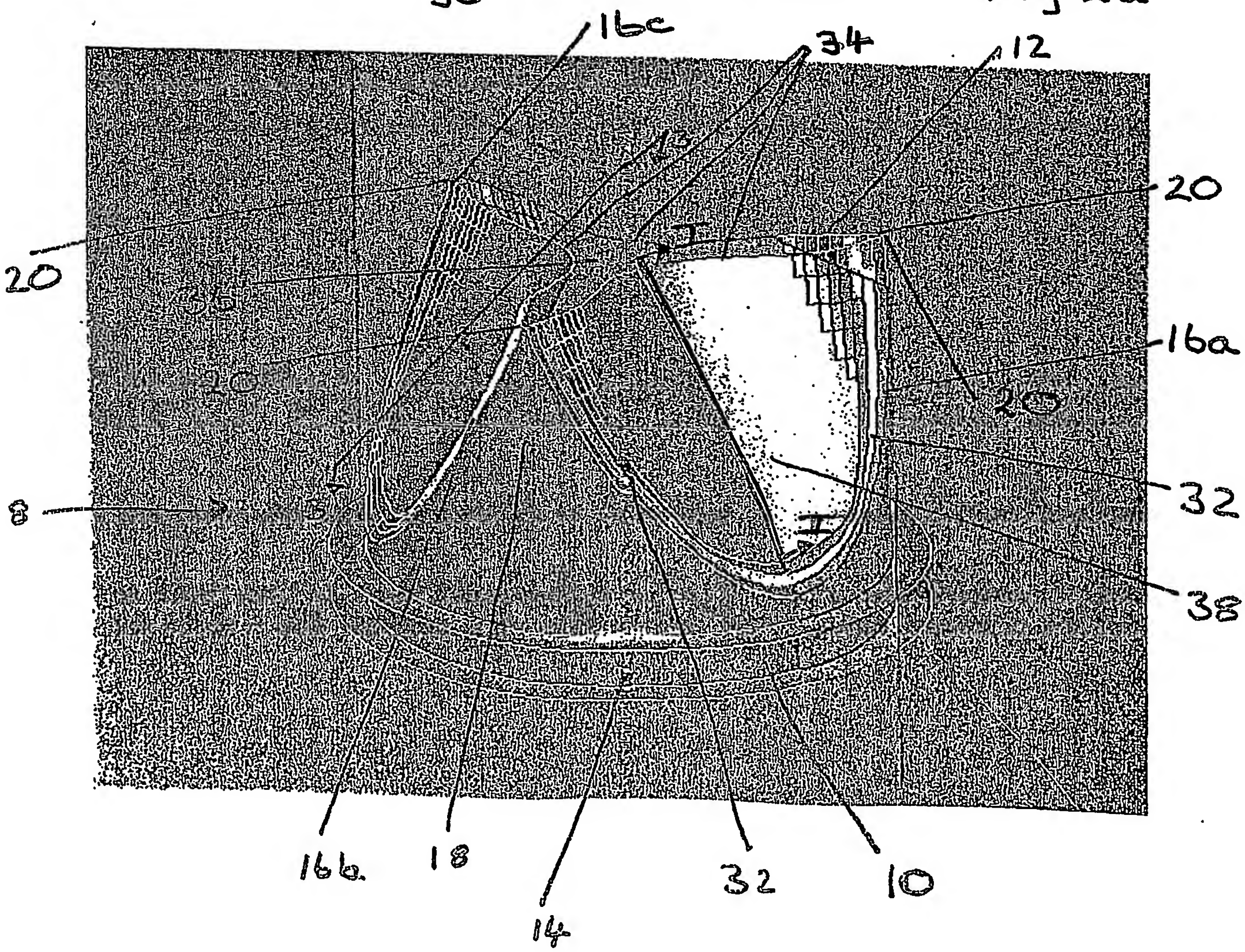

30
20
10
34
30
38
8
20
30
20
y
x

Fig 1

Fig 2a


16c
34
12
20
20
16a
20
32
8
38
16b
18
32
10
14

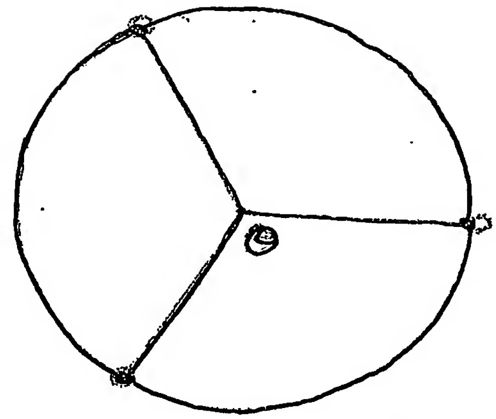


Fig 1 B

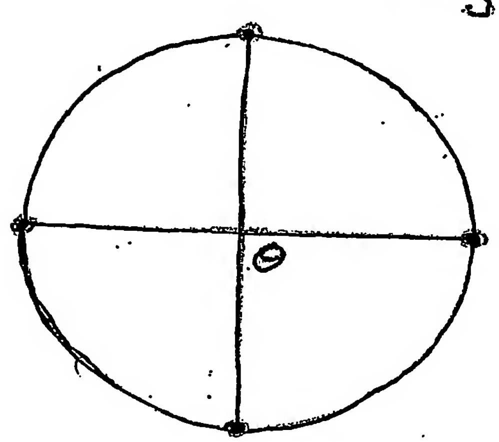


Fig 1 C

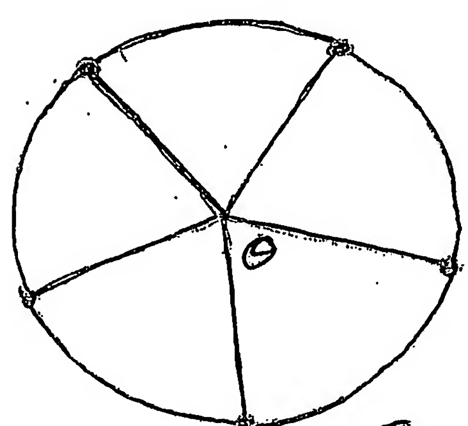


Fig 1 D

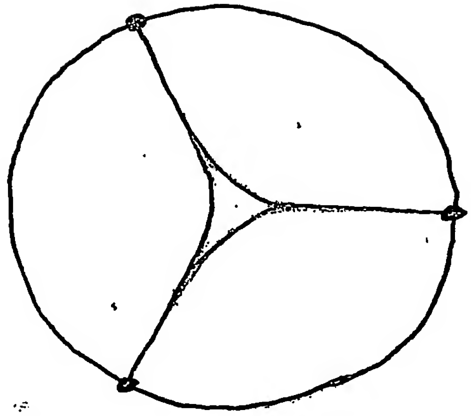


Fig 1 E

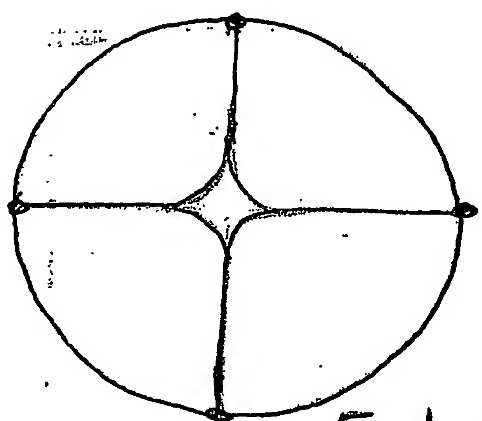


Fig 1 F

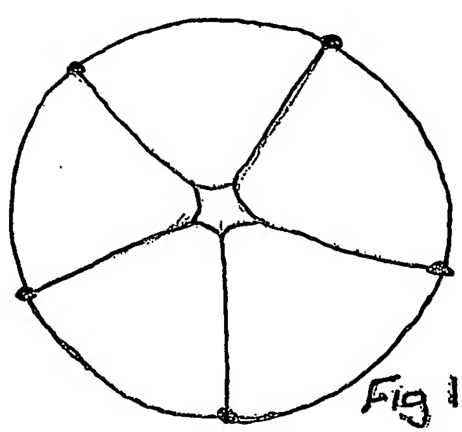


Fig 1 G.

4123

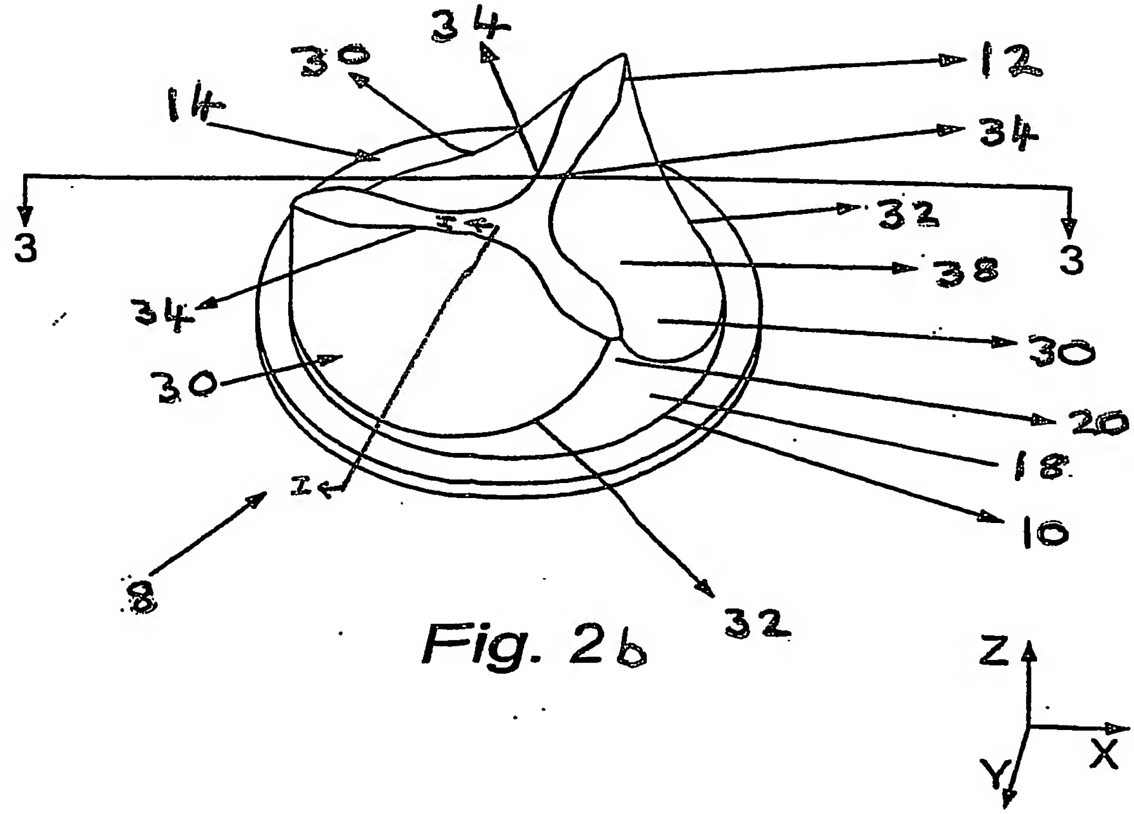


Fig. 2b

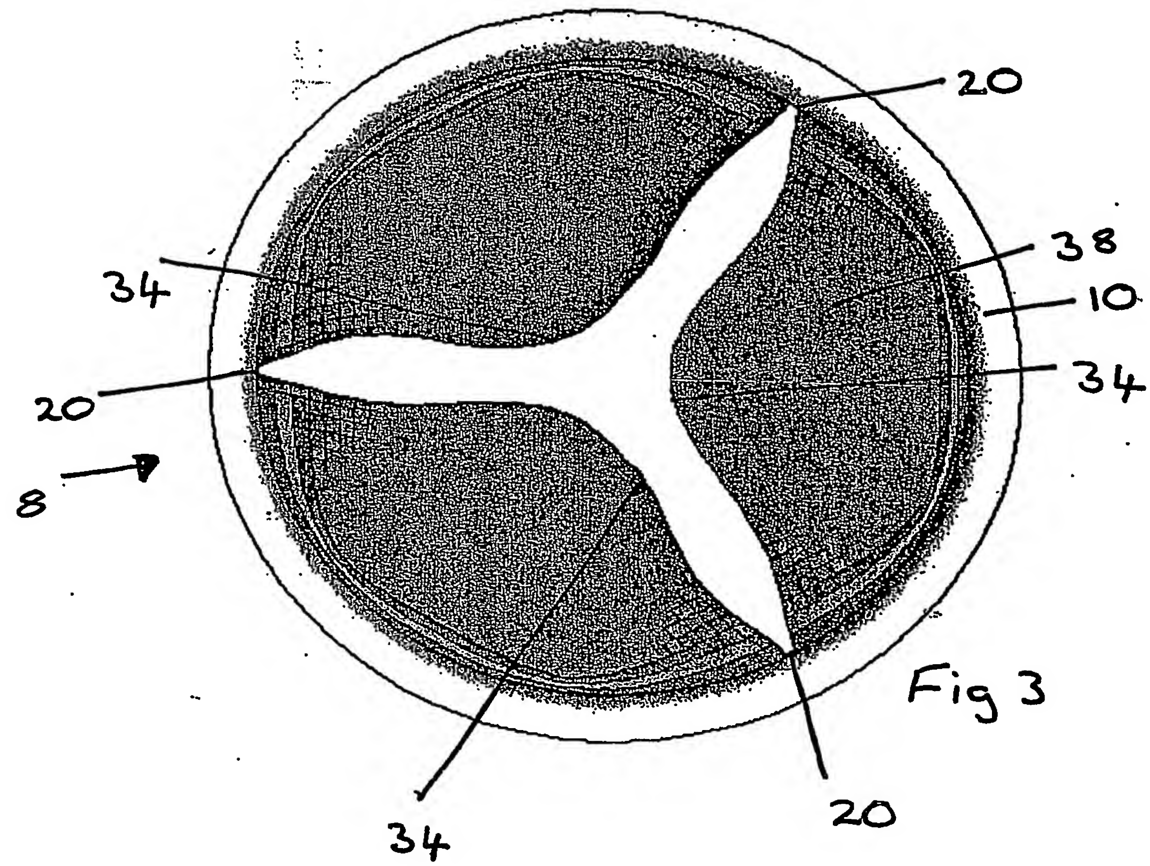


Fig 3

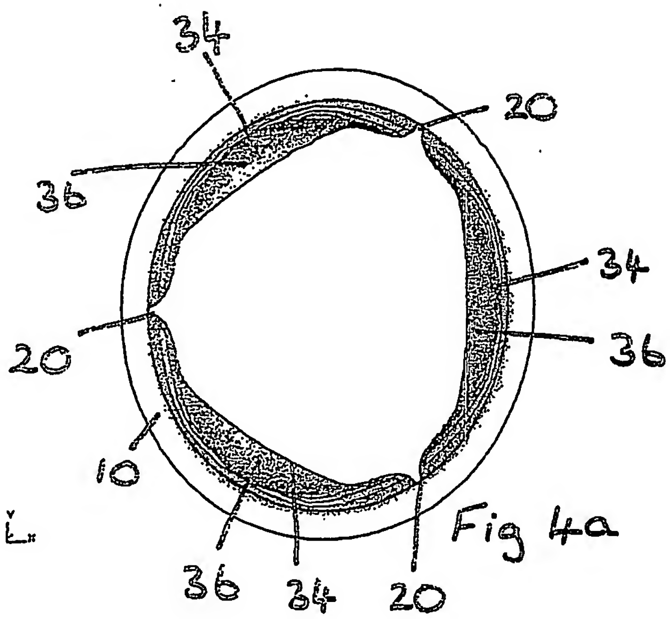


Fig 4a

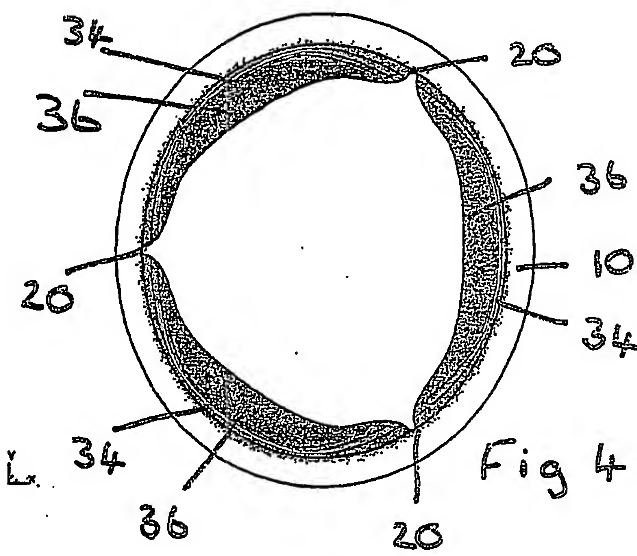


Fig 4c

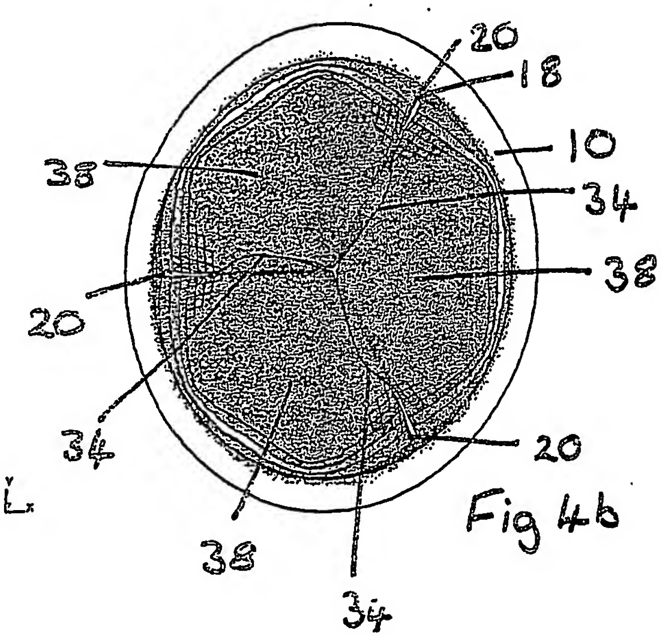


Fig 4b

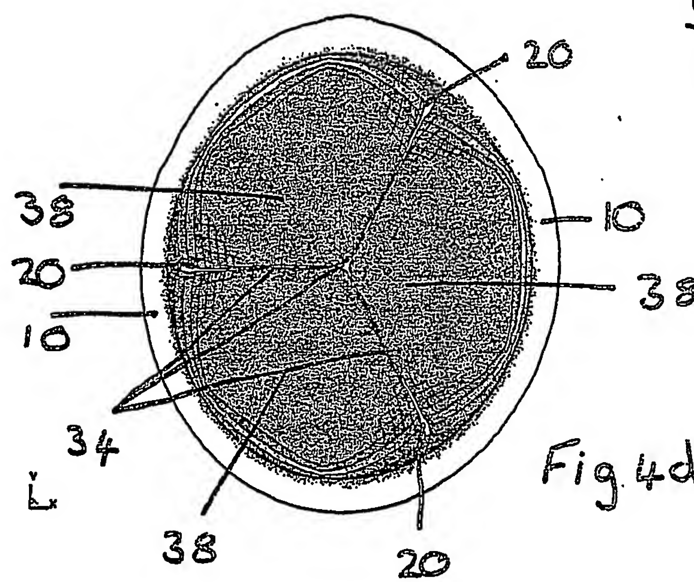


Fig 4d

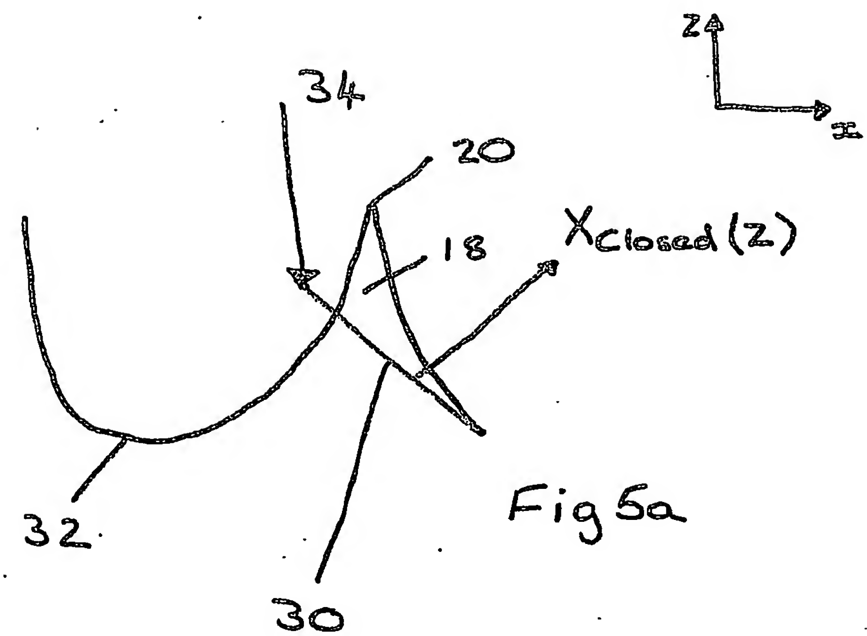


Fig 5a

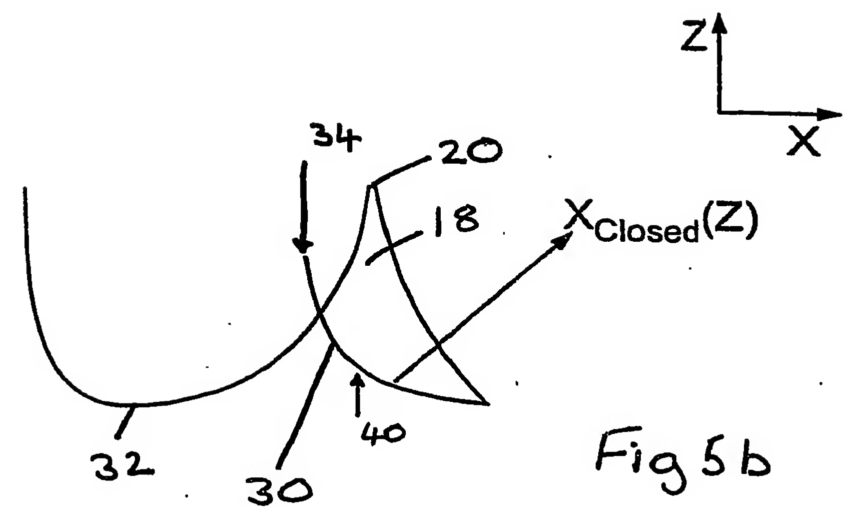


Fig 5b

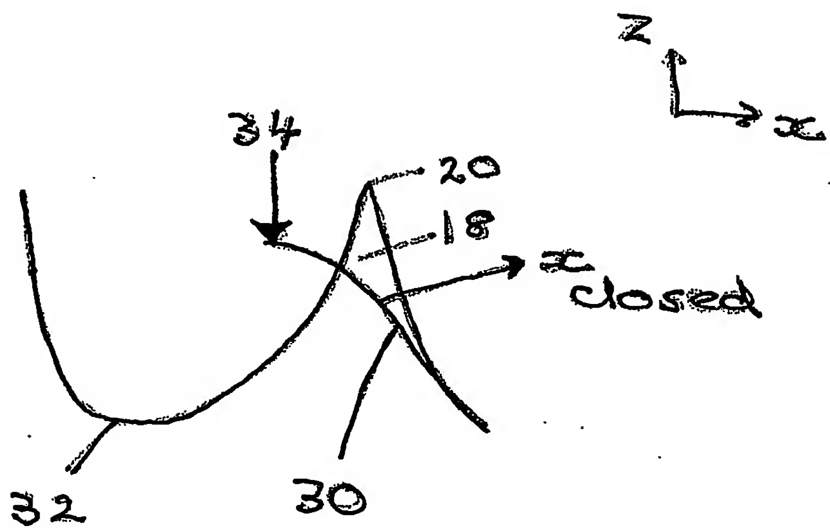


Fig 5c

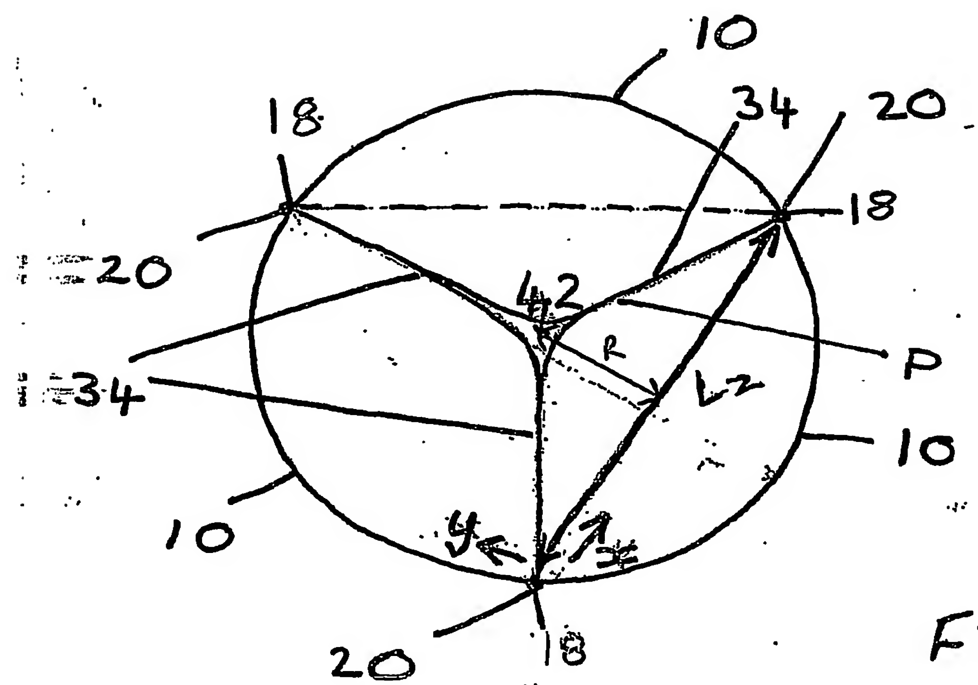


Fig 6

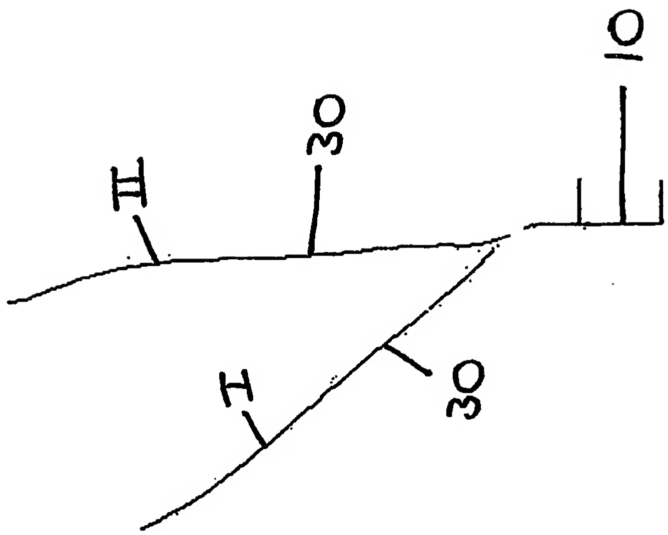


Fig 7b

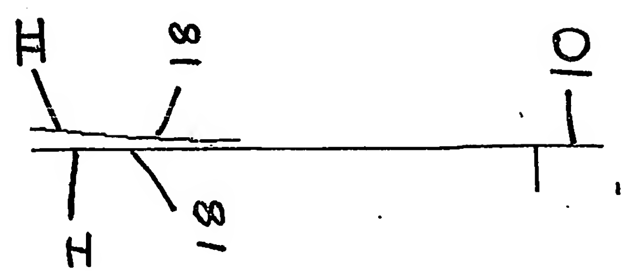


Fig 7a

z
x

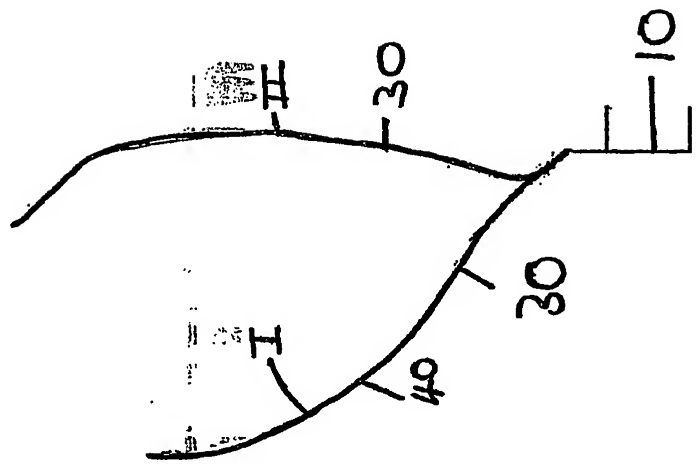


Fig 7d

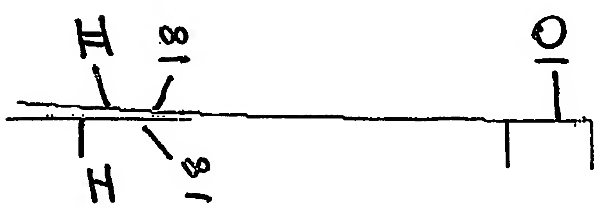


Fig 7c

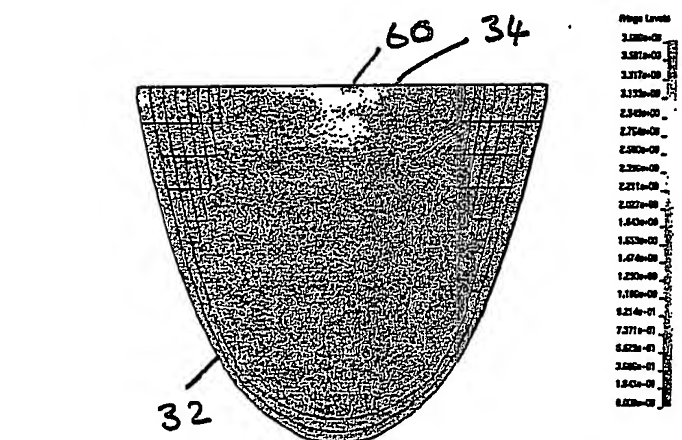


Fig 8a

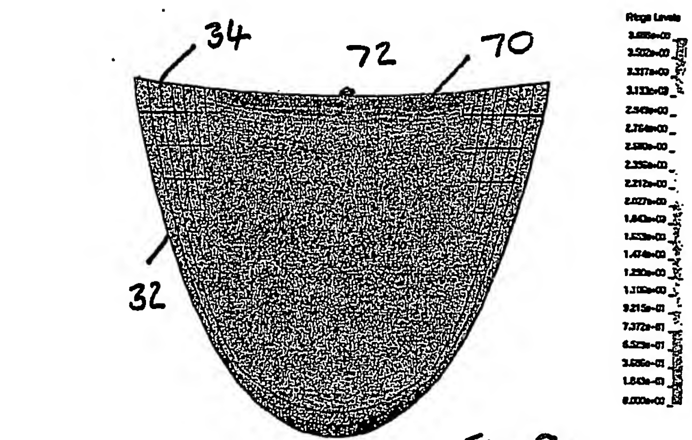


Fig 9a

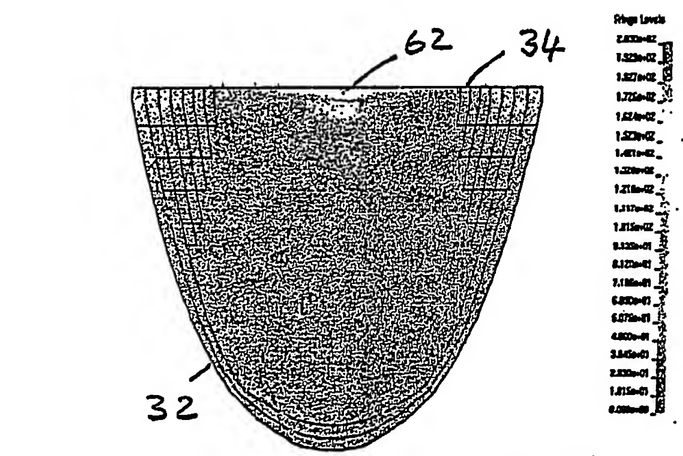


Fig 8b

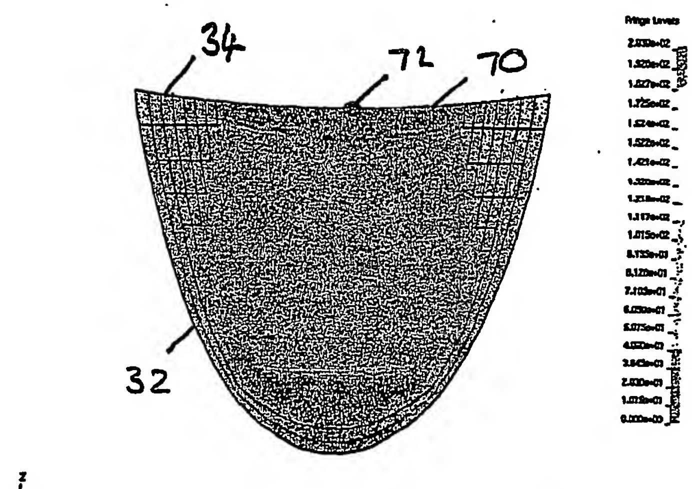


Fig 9b

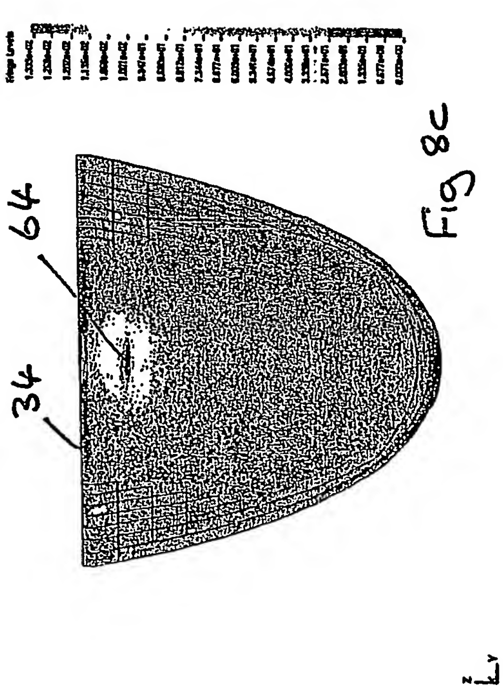


Fig 8c

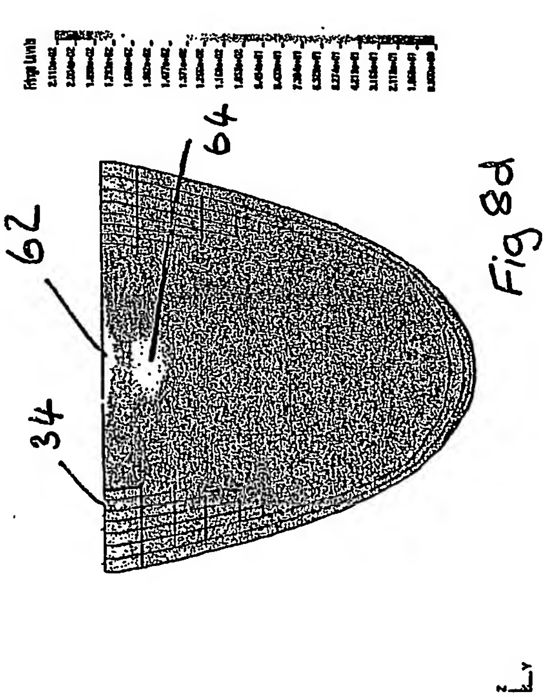


Fig 8d

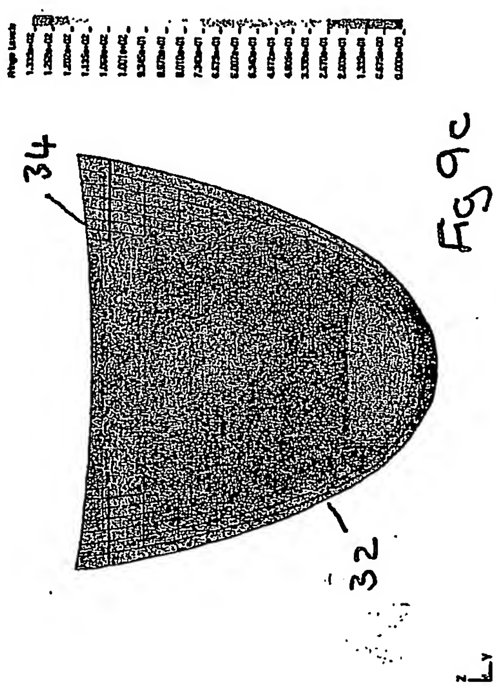


Fig 9c

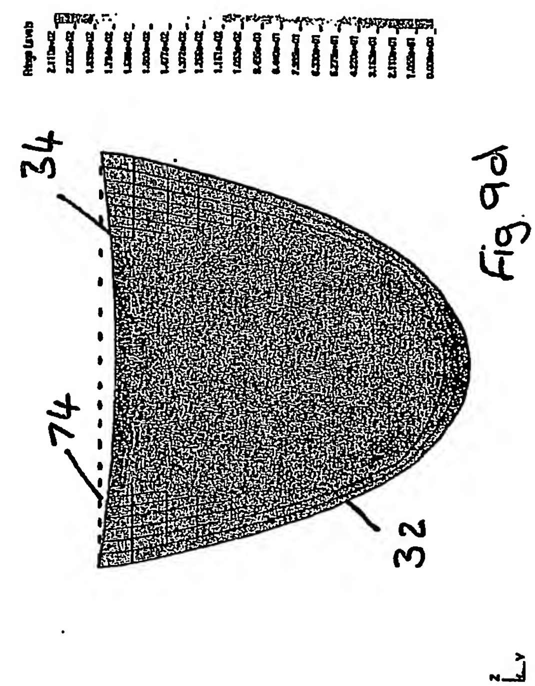


Fig 9d

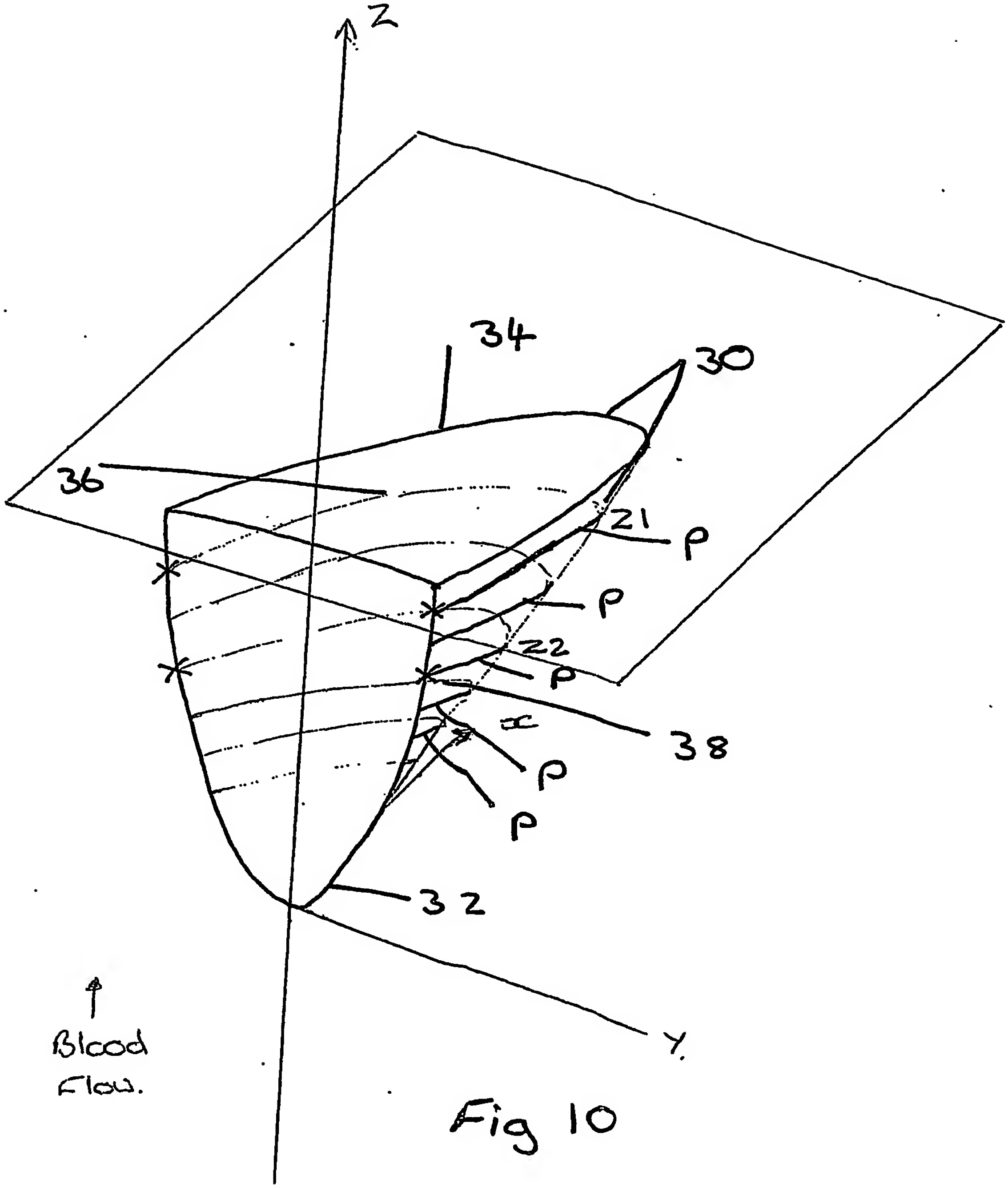


Fig 10

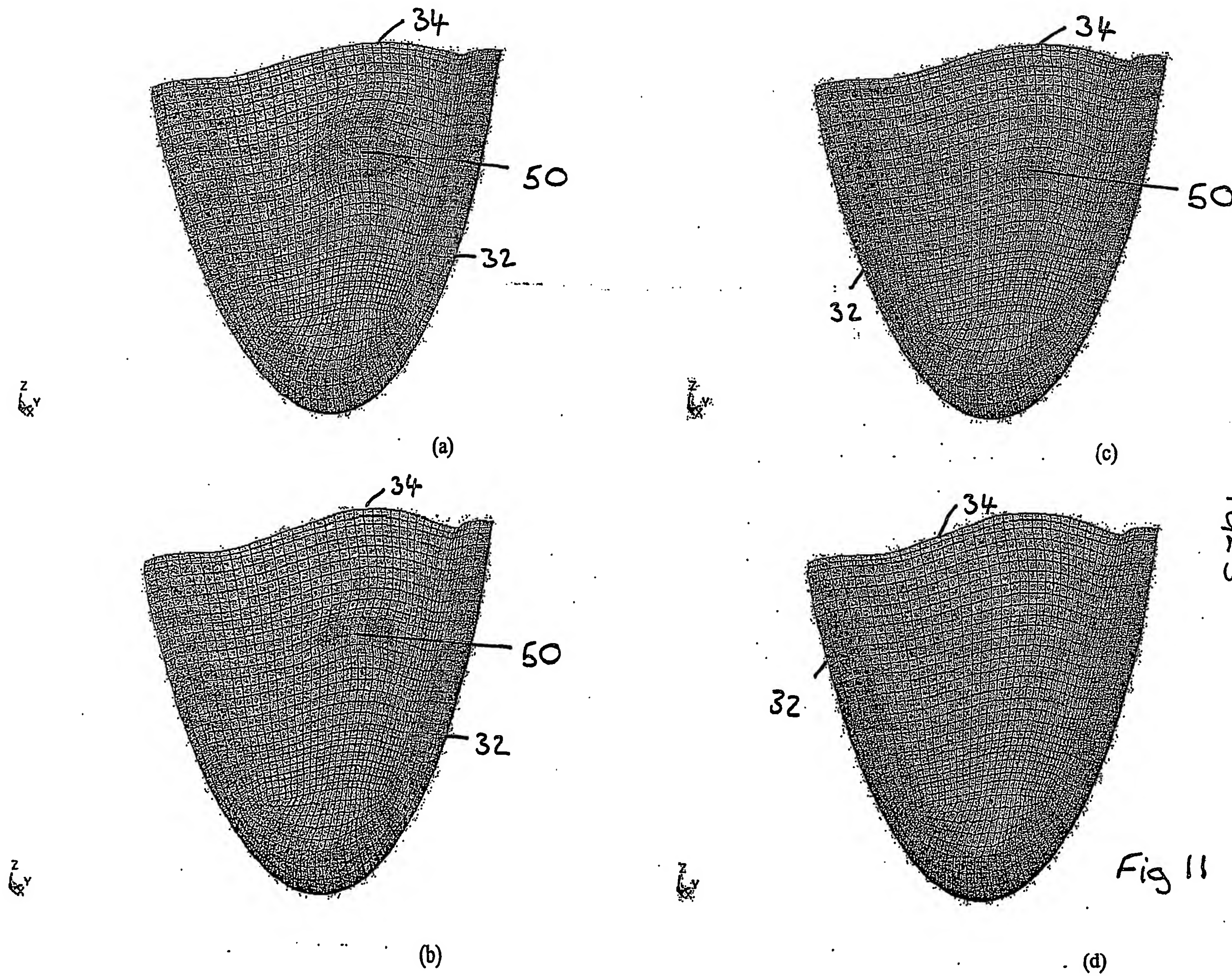


Fig 11

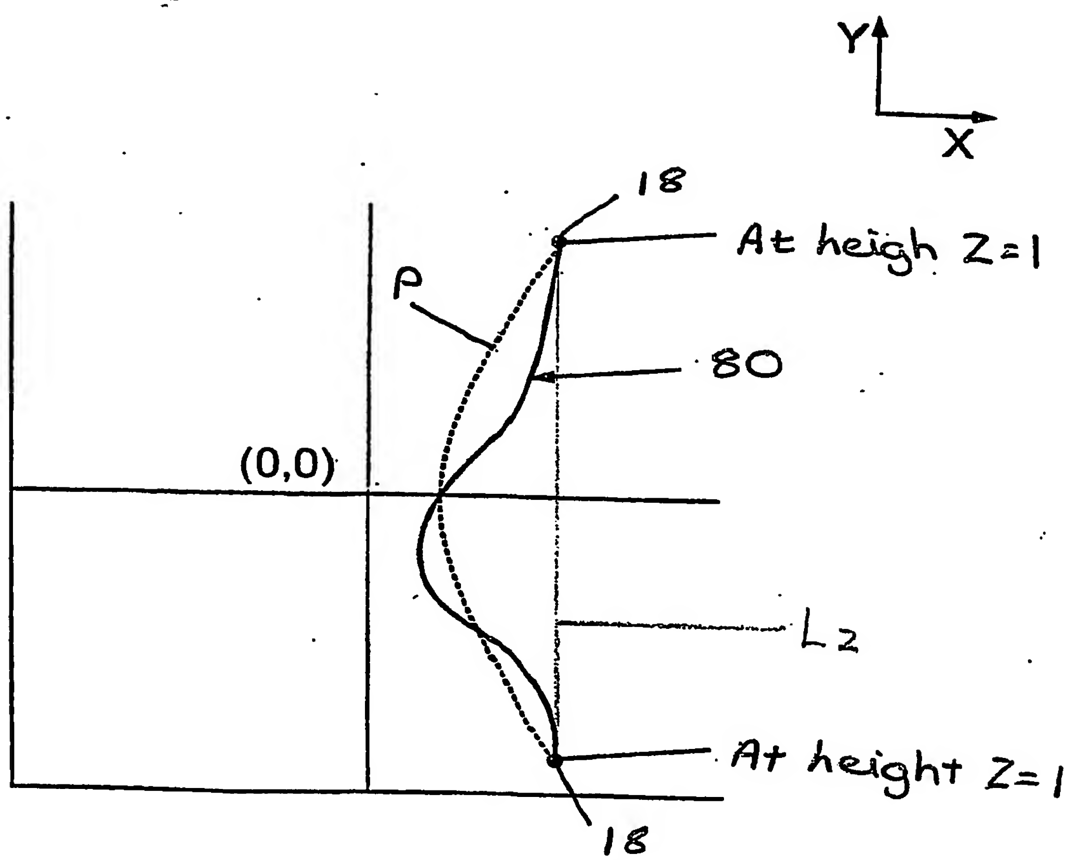


Fig. 12

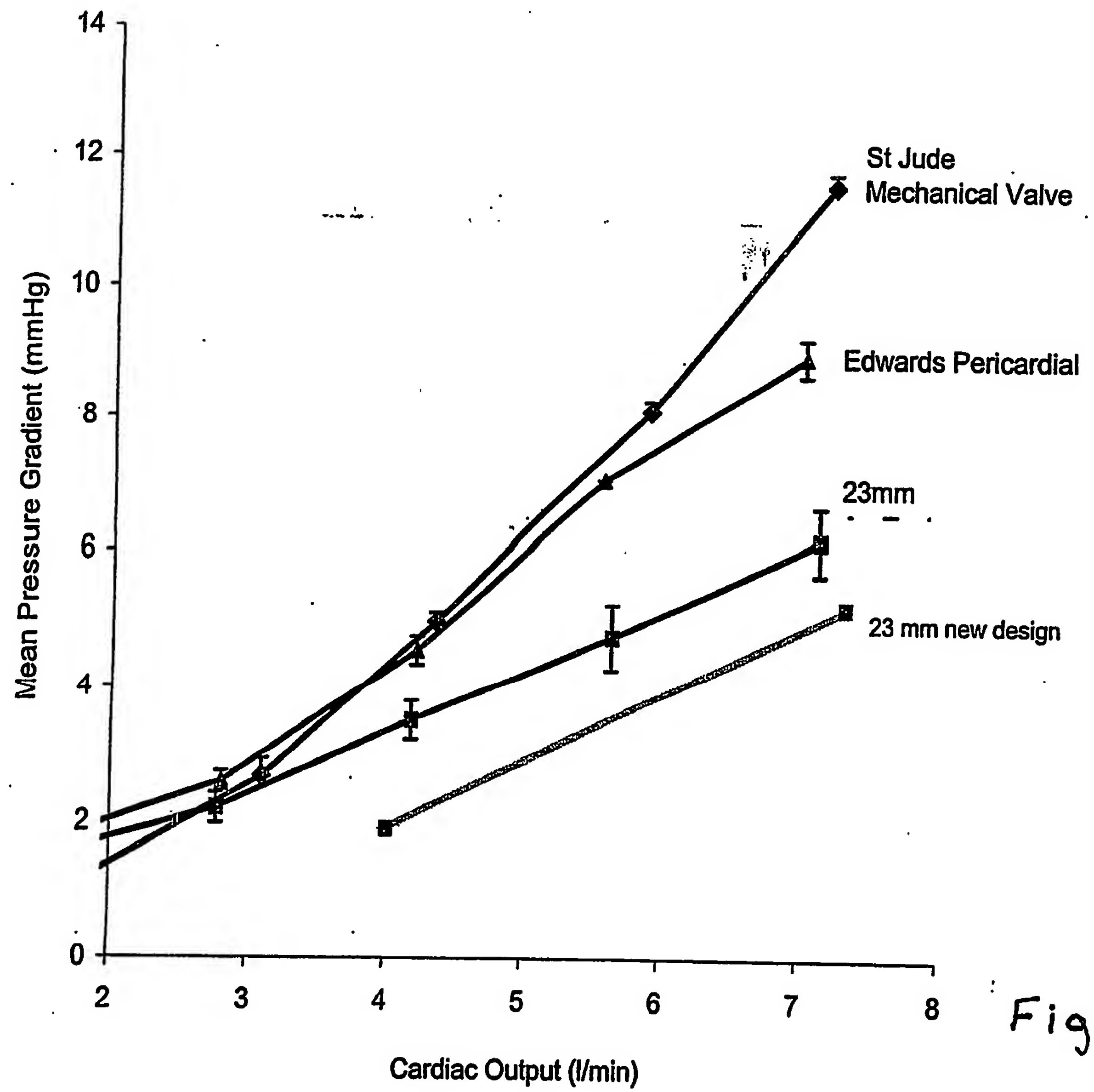

St Jude
Mechanical Valve
Edwards Pericardial
23mm
23 mm new design
Mean Pressure Gradient (mmHg)
Cardiac Output (l/min)
0
2
4
6
8
10
12
14
2
3
4
5
6
7
8

Fig 13

FIGURE 14a

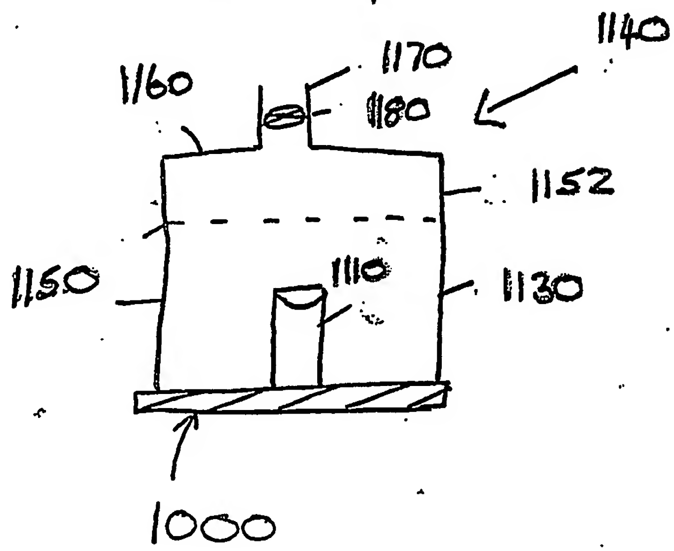


FIGURE 14b

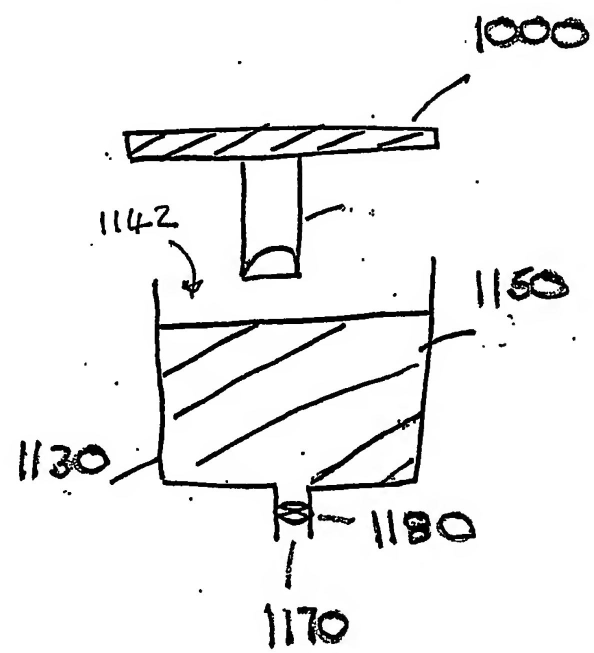


FIGURE 14c

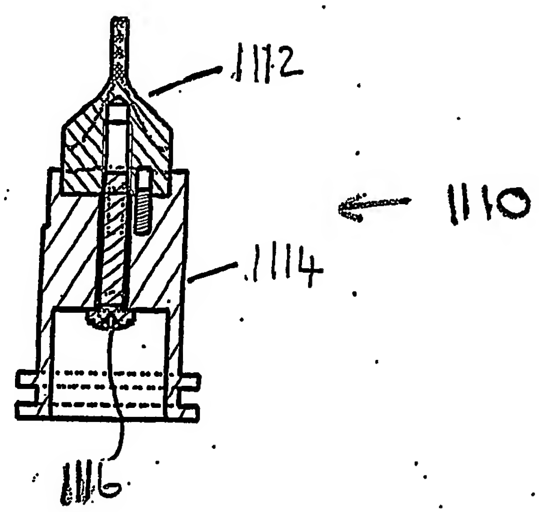


FIGURE 15

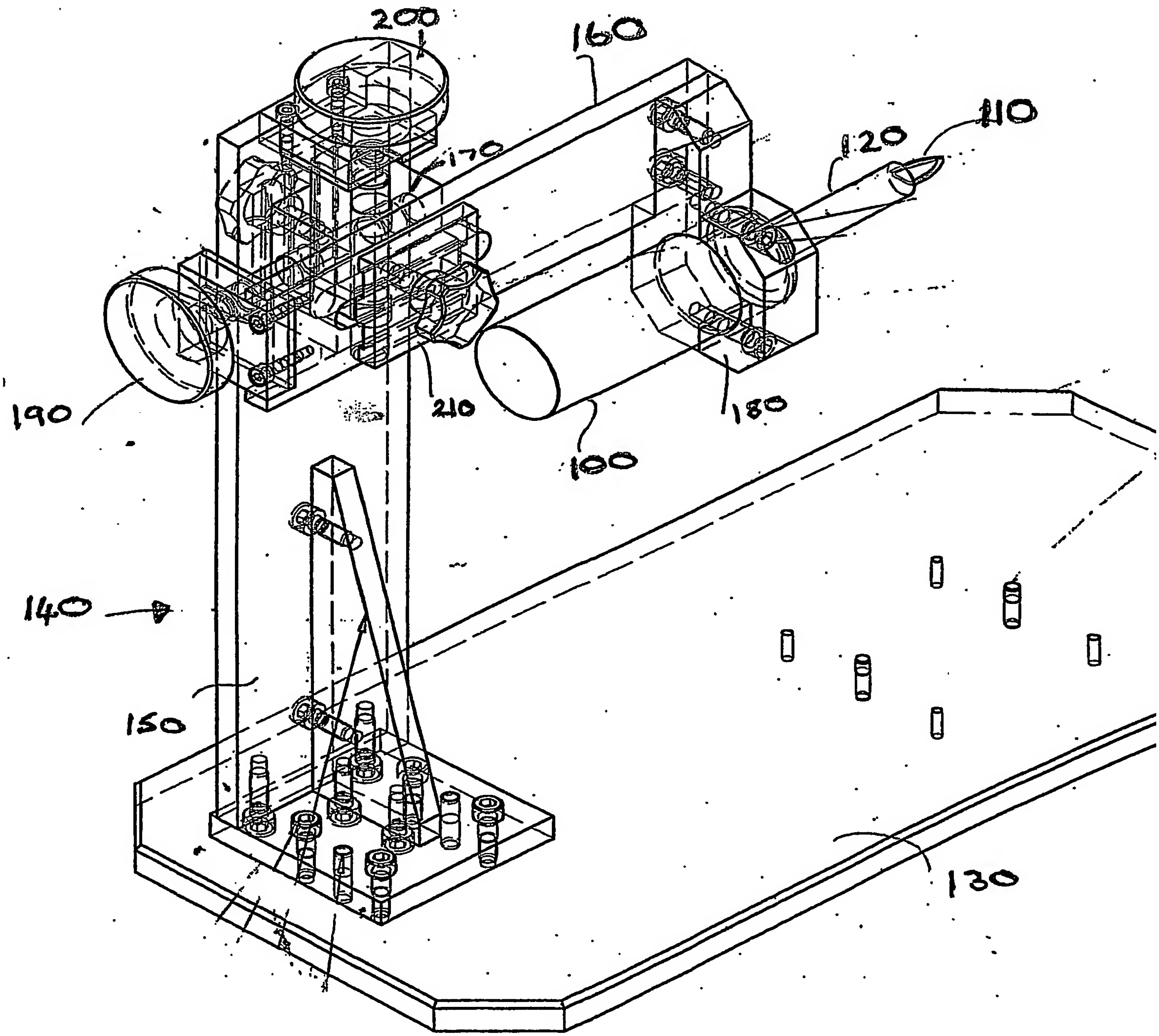


FIGURE 16

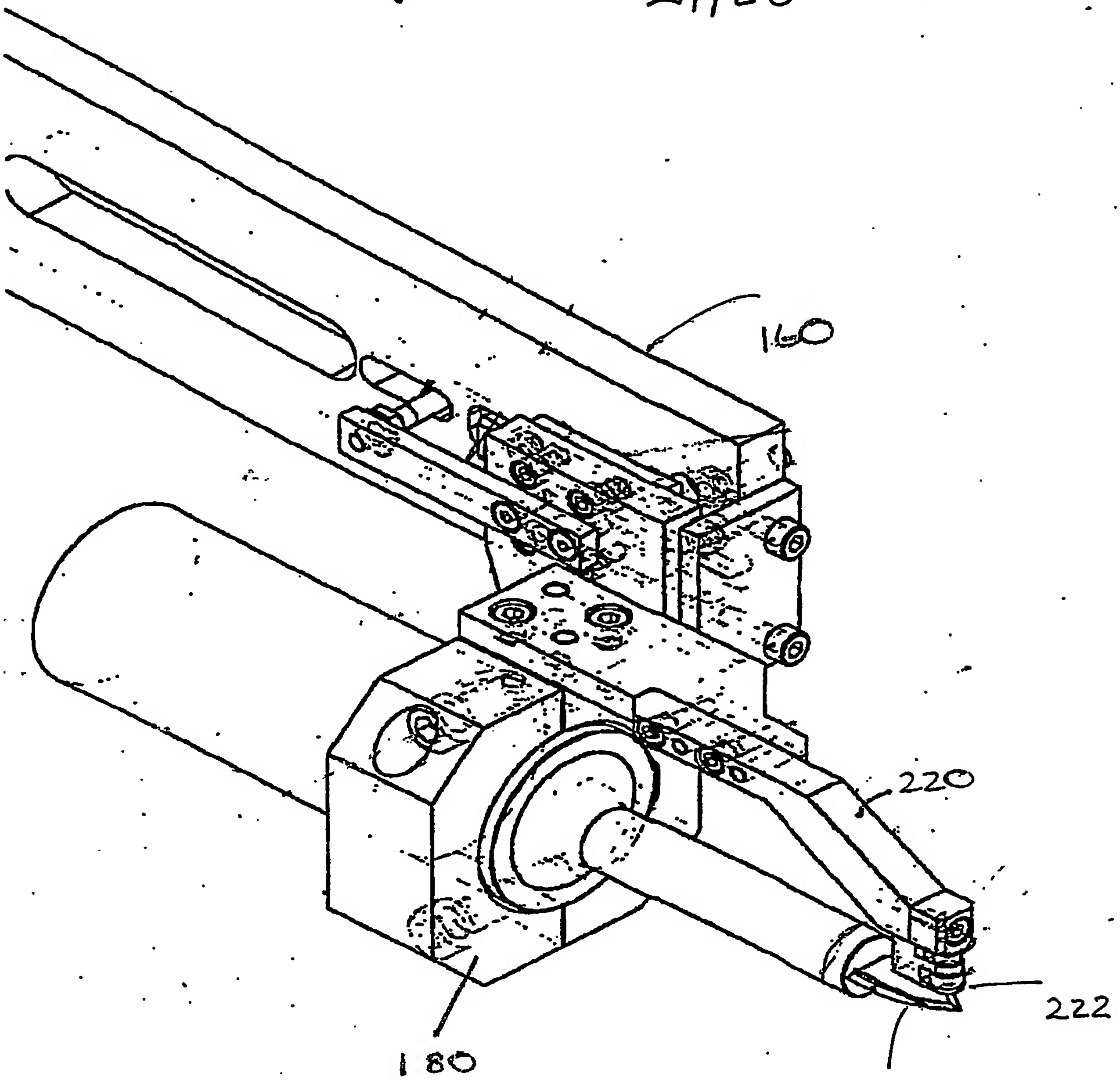


FIGURE 17

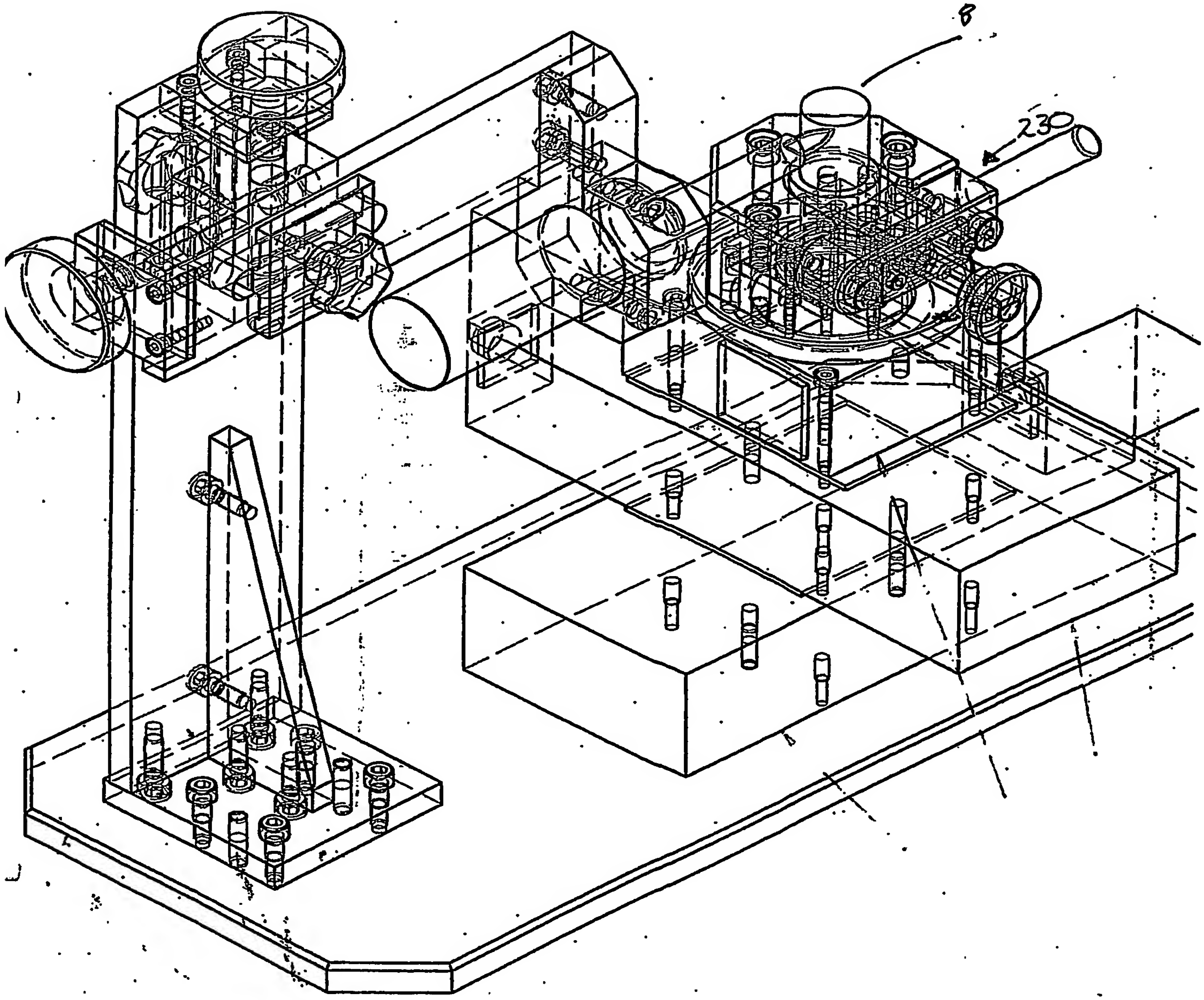


FIGURE 18